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PSYCHOPHARMACOLOGY ABSTRACTS

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

232527 Klosa, Josef. 1 Berlin 37 (Zehlendorf), Janickestr. 13 **/The stability of amphetaminil: syntheses with amphetaminil./** Die Stabilitat von Amphetaminil: Synthesen mit Amphetaminil. Arzneimittel-Forschung (Aulendorf). 25(8):1252-1258, 1975.

The stability of amphetaminil (AN 1), chemically an alpha-phenyl-alpha-((1-methyl-2-phenyl)-ethylamino)-acetonitrile, i.e.,a derivative of alpha-aminonitrile, under experimental conditions of both acid and alkali is demonstrated. It is a uniform substance, and it can be led to derivatives, such as derivatives of acryl which are splittable into the corresponding alpha-amino acid. It yields the corresponding hydantoin, and it is split up by oxidation with hydrogen peroxide in alkaline medium into an amide. These changes and the occurrence of amphetaminil, both under soft and energetic conditions of preparation, make it most improbable to split up easily amphetamine in the organism. Therefore, the existence of amphetamine under chromatographical conditions proves trace elements which are conditioned by use of disproportionately high quantities of solvents. These small quantities are practically irrelevant in case of preparation. They cannot be registered by preparations. 27 references. (Journal abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

226651 Martres, Marie-Pascale; Baudry, Michel; Schwartz, Jean-Charles. Unite de Neurobiologie de l'INSERM (U.109), 2 ter, rue d'Alesia, 75014 Paris, France **Subsensitivity of noradrenaline-stimulated cyclic AMP accumulation in brain slices of d-amphetamine-treated mice.** Nature. 255(5511):731-733, 1975.

An experiment in which male Albino mice were treated with d-amphetamine, a drug experimentally shown to induce an overstimulation of nonadrenergic receptors, resulted in a decreased accumulation of cyclic AMP elicited by nonadrenaline (NA) in cortical slices. This effect seems to be relatively specific to NA. It is suggested that the decreased responsiveness to NA, if it persists after drug withdrawal, may account for the postamphetamine depression and the associated psychological disturbances observed in humans; and it is noted that work is in progress to test this hypothesis. 24 references.

227208 Greenwood, D. T. Biology Department, ICI Ltd, Macclesfield, Cheshire, England **Animal pharmacology of viloxazine (Vivalan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):18-28, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the animal pharmacology of viloxazine (Vivalan), a new antidepressant was discussed. In certain tests predictive of antidepressant activity, such as reserpine - tetrabenazine antagonism and inhibition of the biogenic amine uptake process, viloxazine compared favorably in potency with imipramine. Also in common with imipramine, viloxazine potentiated adrenergic phenomena; but, in contrast to the tricyclic antidepressants, it is virtually devoid of peripheral anticholinergic and antihistamine activity. It reduces body temperature, locomotor activity and susceptibility to electrically and chemically induced convulsions in animals. Although the principal effect of viloxazine on the electrocorticogram is one of desynchrony, it does not exhibit the characteristic behavioral or neurochemical properties of amphetamine or the classical monoamine oxidase inhibitors. 19 references. (Author abstract modified)

227695 Roszkowski, A. P.; Schuler, M. E.; Marx, M.; Edwards, J. A. Institute of Clinical Medicine, Syntex Research, Stanford Industrial Park, Palo Alto, CA 94304 **A central nervous system depressant-antidepressant.** Experientia (Basel). 31(8):960-962, 1975.

Effects on mice of a new tricyclic agent (DMPD) distinguished by an allenyl side chain are reported. Experimental results show antidepressant activity similar to amitriptyline and imipramine as well as marked central nervous system depression. The implications of such dual activity for the clinical treatment of mixed anxiety and depression are discussed. 14 references. (Author abstract modified)

229495 Stolk, Jon M. Dartmouth Medical School, Hanover, NH 03755 **Preclinical studies of rubidium in affective illness.** Psychopharmacology Bulletin. 11(4):78, 1975.

The effect of rubidiumchloride, an alkali metal halide which may have antidepressant properties, on catecholamine physiology and behavior are being investigated, along with the drug's potential nephrotoxicity in rats and dogs. Results of recent studies show that rubidium causes an increase in norepinephrine turnover and increased synthesis of norepinephrine from tyrosine. Investigations of norepinephrine metabolism in brain failed to replicate the findings showing enhancement of normetanephrine formation. However, a study of acute dose/response relationships indicates that norepinephrine metabolism may be decreased by rubidium chloride treatment under certain conditions. The acute decreases in metabolism correlated well with the acute effects of rubidium on rat electroencephalogram (EEG) activity, which showed voltage content and increased rate of spindle events. After subacute rubidium dosing, the EEG pattern reversed, which is consistent with turnover studies and with the proposed use of this drug as an antidepressant. Subacute toxicity studies with dogs revealed no major gross pathological changes, but indicated definite areas of concern requiring further research before clinical use can be considered. (Journal abstract modified)

232528 Coscia, L.; Causa, P.; Giuliani, E. Research Laboratories of Richardson-Merrell S. P. A., via Peitro Castellino 111, I-80131 Naples, Italy **New tricyclic enamine derivatives with CNS depressant properties.** Arzneimittel-Forschung (Aulendorf). 25(8):1261-1265, 1975.

Sixty three tricyclic enamine derivatives were synthesized and pharmacologically tested using mice and rats. Many of the screened compounds showed remarkable central nervous system (CNS) depressant chlorpromazine like activities. The compounds no. 9 (substituents CH3, Cl, H), 18 (substitutents CH3, F, H) and 26 (substituents CH3, OCH3, H) caused the most interesting results and were studied in comparison with chlorpromazine and chlordiazepoxide. They were submitted to further studies in view of trials in humans. 10 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

225570 Takahashi, R. N.; Karniol, I. G. Depto. de Psicobiologia, Escola Paulista de Medicina, R. Botucatu 862, BR-04023, Sao Paulo, Brazil **Pharmacological interaction between cannabinol and delta9-tetrahydrocannabinol.** Psychopharmacologia (Berlin). 41(3):277-284, 1975.

Rabbits, rats and mice were used in a study of the pharmacological action of delta9-tetrahydrocannabinol (delta9-THC), cannabinol (CBN), and mixtures of both. The tests were: 1) corneal arreflexia in rabbits, 2) climbing rope, open field, irritability and aggressiveness after Rapid Eye Movement (REM) sleep deprivation in rats, and 3) catatonia, analgesia and sleeping time in mice. It was found that a delta9-THC + CBN mixture created a synergistic effect on most of the depressant effects. Results indicate that CBN mimicked the effects of delta9-THC in several tests, although the CBN was generally less active; that CBN did not interfere with, or only slightly inhibited the excitatory effects of delta9-THC; and that in the one peripheral test, CBN did not alter the delta9-THC effect. 24 references. (Author abstract modified)

225572 Goudie, A. J.; Kelley, Maureen; Taylor, M.; Wheeler, T. J. University of Liverpool, P.O. Box 147, Liverpool, L69 3BX, England **Acute sedative properties of SKF 525A in rats: implications for its use as a metabolism inhibitor in the study of psychoactive drugs.** Psychopharmacologia (Berlin). 41(3):291-294, 1975.

Acute sedative properties of SKF 525A in rats at doses of 25 and 50 mg/kg injected intraperitoneally were experimentally studied. Behavioral effects were assessed by Time Sampling Behavioral Categorization of exploratory behavior and by activity measurements obtained with an ultrasonic motion recorder. Results demonstrate that SKF 525A has sedative properties in rats at doses which are conventionally used to inhibit metabolism of a wide range of drugs. Results are discussed relative to the use of SKF 525A as a metabolism inhibitor in the study of psychotropic drug action. 16 references. (Author abstract modified)

225574 Doggett, Neil S. Welsh School of Pharmacy, UWIST, Cardiff, Great Britain **The effect of ouabain and digitoxin on hexobarbitone sleeping time in the mouse.** Psychopharmacologia (Berlin). 41(3):305-308, 1975.

The effect of ouabain and digitoxin on sleeping time and on duration of loss of righting reflex produced by hexobarbitone in mice pretreated with the liver microsomal enzyme inhibitor SKF 525A was studied. Both ouabain and, to a greater extent, digitoxin produced a dose dependent potentiation of the activity of hexobarbitone. These results, which are considered to confirm and extend previous observations, are explained by a direct interaction at the level of the central nervous system and by a modified distribution of the barbiturate. Results are discussed in terms of the possibility of such an interaction in the clinic. 11 references. (Author abstract)

226397 Daniels, J. D.; Pettigrew, J. D. Division of Biology, California Institute of Technology, Pasadena, CA 91125 **A study of inhibitory antagonism in cat visual cortex.** Brain Research (Amsterdam). 93(1):41-62, 1975.

The effects of an antagonist of gamma-aminobutyric acid (GABA) on the response properties of cat visual cortex neurons were tested, using a computer controlled stimulus presentation system to assess quantitatively the changes in receptive field organization after administration of the drug. Complex cells were found to be most affected, increasing both evoked and spontaneous activity and losing some of their specificities for stimulus parameters such as orientation and direction. Results are discussed in relation to the synaptic anatomy of the cortex. It is concluded that a class of stellate cells using GABA is a likely candidate for the transmitter of some intracortical inhibition. 48 references. (Author abstract modified)

226398 Barker, Jeffery L. National Institute of Child Health and Human Development, NIH, Bethesda, MD 20014 **Inhibitory and excitatory effects of CNS depressants on invertebrate synapses.** Brain Research (Amsterdam). 93(1):77-90, 1975.

Inhibitory and excitatory effects of central nervous system depressants on invertebrate synapses were studied. Lobsters, crayfish, and snails were used. Pentobarbital, chloralose, chloroform, ethanol, and urethane were studied with respect to membrane properties and synaptic activity of crustacean neuromuscular junction preparations and molluscan neurons. Results in these invertebrate systems were viewed as insightful into the cellular basis of the depressant and excitatory effects of these agents. 68 references. (Author abstract modified)

226399 Emson, Piers Christopher; Joseph, Michael Hampden. MRC Brain Metabolism Unit, Department of Pharmacology, Edinburgh University, Edinburgh EH8 9JZ, Great Britain **Neurochemical and morphological changes during the development of cobalt-induced epilepsy in the rat.** Brain Research (Amsterdam). 93(1):91-110, 1975.

Neurochemical and morphological changes during the development of cobalt induced epilepsy in the rat were studied. Histological examination after implantation of cobalt gelatine pellets into the frontal cortex showed a necrotic lesion with terminal and fiber degeneration in brain areas connected with the frontal cortex. Enzyme levels were changed. It is concluded that cobalt induced epilepsy is associated with relatively selective loss of neuronal tissue and provides a useful model for further investigation relevant to clinical epilepsy. 45 references. (Author abstract modified)

226400 Gallager, D. W.; Sanders-Bush, E.; Aghajanian, G. K.; Sulser, F. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37217 **An evaluation of the use of intraventricularly administered (3H)5-hydroxytryptamine as a marker for endogenous brain 5-hydroxytryptamine.** Brain Research (Amsterdam). 93(1):111-122, 1975.

An evaluation of the use of intraventricularly administered (3H)5-hydroxytryptamine (3H-5-HT) as a marker for endogenous brain 5-hydroxytryptamine (5-HT) is reported. Following injection in rats of a small amount of 3H-5-HT, the amount of radioactivity in telencephalic structures on the injected side was six to seven times larger than that in corresponding areas on the opposite side, and a multiphasic disappearance from whole brain or midbrain was found after injection of the labeled amine. 3H-5-HT injected labels were relatively resistant to the depleting effect of the reserpine like drug, Ro4-1284, and to that elicited by destruction of the midbrain raphe nuclei. Results indicate that intraventricular injection of 3H-5-HT leads to the formation of artifactual pools which are not present if the amine is synthesized in vivo. 30 references. (Author abstract modified)

226401 Neckers, Leonard; Sze, Paul Y. Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Regulation of 5-hydroxytryptamine metabolism in mouse brain by adrenal glucocorticoids.** Brain Research (Amsterdam). 93(1):123-132, 1975.

The effects of glucocorticoid hormone on the metabolism of brain 5-hydroxytryptamine (5-HT) were studied in mice. Injection of hydrocortisone acetate (HCA) accelerated accumulation of 5-HT in whole brain after inhibition of monoamine oxidase activity by pargyline. The hormone did not appear to change brain tryptophan hydroxylase or 5-hydroxytryptophan decarboxylase activity. However, tryptophan levels in brain were elevated by 50% within 1 hour after treatment with HCA, with effect of HCA on brain tryptophan levels localized mainly in nerve endings. Results demonstrate that glucocorticoids may directly act on nerve terminals in the regulation of 5-HT synthesis through an action on the uptake of tryptophan. 31 references. (Author abstract modified)

226406 Spano, P. F.; Kumakura, K.; Tonon, G. C.; Govoni, S.; Trabucchi, M. Institute of Pharmacology and Pharmacognosy, University of Milan, Milan, 20129 Italy **LSD and dopamine-sensitive adenylate-cyclase in various rat brain areas.** Brain Research (Amsterdam). 93(1):164-167, 1975.

An investigation, using rats, to determine whether dopa (D) LSD directly and selectively stimulates dopamine (DA) sensitive adenylate cyclase in styiatum and in other areas of the limbic system which appear to be more strictly linked to perception, feeling and emotional behavior is reported. Results indicate a common site of action for DA and LSD on the DA sensitive adenylate cyclase system. Results also support the hypothesis of a direct effect of LSD on the DA sensitive adenylate cyclases which have been associated with the dopaminergic receptors in brain. It is considered significant that these areas are part of the limbic brain which may play an important role in the psychotomimetic action of LSD. 20 references.

226407 Enna, S. J.; Kuhar, Michael J.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Regional distribution of postsynaptic receptor binding for gamma-aminobutyric acid (GABA) in monkey brain.** Brain Research (Amsterdam). 93(1):168-174, 1975.

An evaluation is reported of the regional distribution of the gamma-aminobutyric acid (GABA) synthesizing enzyme glutamic acid decarboxylase (GAD), the synaptosomal uptake of GABA, sodium independent binding of GABA to its postsynaptic receptor sites, and the sodium dependent GABA binding process. Findings reveal that sodium independent GABA receptor binding correlates with synaptosomal uptake of GABA and with GAD activity, but not with sodium dependent GABA binding. 27 references.

226726 Papeschi, Raffaello; Theiss, Peter. Ospedale Psichiatrico Provinciale, 55050 Maggiano, Lucca, Italy **The effect of yohimbine on the turnover of brain catecholamines and serotonin.** European Journal of Pharmacology (Amsterdam). 33(1):1-12, 1975.

The effect of yohimbine on the turnover of brain catecholamines and serotonin was examined in rats. Yohimbine moderately increased the depletion of brain dopamine (DA) after alpha-methyl-p-tyrosine (AMT) only when the two drugs were given at the same time; the baseline concentration of brain homovanillic acid (HVA) and its accumulation after probenecid were strongly increased by yohimbine. Yohimbine markedly decreased the concentration of brain noradrenaline (NA), both when given alone and before or at the same time as AMT; when it was given at an increasing interval after AMT, the effect became progressively smaller. The baseline concentration of brain 3-methoxy-4-hydroxyphenylethyleneglycol sulphate and its accumulation after probenecid were increased by yohimbine; this effect was not as marked as that on HVA and was proportional to the quantity of NA depleted in the AMT method. The accumulation of brain 5-hydroxyindoleacetic acid after probenecid was decreased by yohimbine pretreatment. 29 references. (Author abstract)

226727 Westerink, Ben H. C.; Korf, Jakob. Department of Clinical Chemistry, Groningen University, The Netherlands **Influence of drugs on striatal and limbic homovanillic acid concentration in the rat brain.** European Journal of Pharmacology (Amsterdam). 33(1):31-40, 1975.

Homovanillic acid (HVA) was measured in the corpus striatum and the limbic structures nucleus accumbens and olfactory tubercle of the rat, under normal conditions and after different drug treatments. Clozapine, thioridazine, morphine and physostigmine induced a similar percentage HVA increase in the three brain structures studied. Haloperidol and pimozide induced a higher percentage increase of HVA in the corpus striatum and nucleus accumbens. Probenecid induced a significantly higher percentage accumulation of HVA in the limbic structures, especially in the olfactory tubercle. The HVA rise seen after haloperidol was suppressed by pretreatment with p-chlorophenylalanine or amino-oxyacetic acid in all structures studied. After atropine or trihexyl-phenidyl treatment the HVA rise induced by haloperidol was slightly suppressed in the limbic structures only. Results suggest that not only under normal conditions but also after treatment with various types of drugs, dopamine metabolism as reflected by the HVA levels, is closely related in the different rat brain structures. 44 references. (Author abstract)

226728 Kleinlogel, Horst; Scholtysik, G.; Sayers, A. C. Research Institute Wander, Sandoz Research Unit, Berne, Switzerland **Effects of clonidine and BS 100-141 on the EEG sleep pattern in rats.** European Journal of Pharmacology (Amsterdam). 33(1):159-163, 1975.

The effects of the peripheral and central alpha adrenoceptor stimulant and antihypertensive agents clonidine and BS 100-141 (N-amidino-2(2,6-dichlorophenyl) acetamide HC1) on electroencephalographic sleep patterns in rats and on blood pressure in pithed rats were investigated. Whereas both compounds abolished paradoxical sleep (PS), clonidine, in contrast to BS 100-141, markedly increased the sleeping time. Both drugs caused a dose dependent increase in the blood pressure of pithed rats. The pressor action was abolished by alpha adrenoceptor blocking agent phentolamine, but was not influenced by reserpine, indicating a direct stimulation of vascular alpha adrenoceptors by both drugs. It is suggested that sedation or sleep induction by adrenergic drugs cannot be explained exclusively by an action on central alpha adrenoceptors. The findings suggest that such an action may be involved in the modulation of PS. 20 references. (Author abstract)

226739 Sorimachi, Masaru; Kataoka, Kiyoshi. Department of Physiology, Ehime University School of Medicine, Matsuyama 790, Japan **High affinity choline uptake: an early index of cholinergic innervation in rat brain.** Brain Research (Amsterdam). 94(2):325-336, 1975.

The uptake of (3H)choline was investigated in nuclei free homogenates or crude synaptosomal fractions (P2) from rat brain under various stages of development. A comparable sensitivity of uptake to treatment by hyposmotic shock suggested the involvement of synaptosomal populations in choline uptake in immature as well as in adult brains. On these assumptions,

the developmental changes of cholinergic synaptogenesis were examined in five distinct regions of the brain. It was found that the synaptogenesis begins several days earlier than the increase of choline acetyltransferase (ChAc) level in the frontal cortex, the hippocampus, the superior colliculus and the cerebellum. It is concluded that the increase of ChAc in the terminal rich regions is delayed by the axoplasmic flow; therefore, the earlier index of cholinergic synaptogenesis in these regions is the high affinity uptake activity rather than the enzyme activity. 20 references. (Author abstract modified)

226761 Horn, Alan S.; Post, Michael L.; Kennard, Olga. MRC Neurochemical Pharmacology Unit, University of Cambridge, Hills Road, Cambridge, England **Dopamine receptor blockade and the neuroleptics, a crystallographic study.** Journal of Pharmacy and Pharmacology (London). 27(8):553-563, 1975.

The X-ray structures of 12 drugs of the tricyclic class having varying pharmacological profiles were examined in detail in an attempt to rationalize the known structure - activity relations of neuroleptic drugs with respect to their ability to block dopamine receptors in the brain. Further evidence is presented in support of the theory that the neuroleptics are able to block dopamine recepotrs because of a conformational complementarity between certain portions of these drugs and dopamine. 67 references. (Author abstract)

226762 Kaymakcalan, S.; Ercan, Z. S.; Turker, R. K. Department of Pharmacology, Faculty of Medicine, University of Ankara, Ankara, Turkey **The evidence of the release of prostaglandin-like material from rabbit kidney and guinea-pig lung by (-)-trans-delta9-tetrahydrocannabinol.** Journal of Pharmacy and Pharmacology (London). 27(8):564-568, 1975.

Evidence is presented that the injection of (-)-trans-delta9-tetrahydrocannabinol (THC) through the renal artery caused a decrease in perfusion pressure and an increase in urine produced by the isolated perfused rabbit kidney. Both effects of THC are inhibited by the prior addition of aspirin to the perfusion medium. THC also induced a dose dependent increase in perfusion pressure on the isolated perfused lung of guinea-pig, and the effluent from the lung produced a contraction on the isolated continuously superfused rat stomach fundus strip. These effects are prevented by the pretreatment of the lung with aspirin which inhibits the production of prostaglandins (PG) and SC 19220 which inhibits the pharmacological effects of PG. 17 references. (Author abstract)

226763 List, Alan F.; Bartram, Scott F.; Nazar, Barry L.; Harclerode, Jack. Department of Biology, Bucknell University, Lewisburg, PA 17837 **Interactions of delta9-tetrahydrocannabinol, adrenal steroids, and ethanol.** Journal of Pharmacy and Pharmacology (London). 27(8):606-607, 1975.

The interactions of delta9-tetrahydrocannabinol (THC), adrenal steroids and ethanol were examined in mice. In all instances, endogenous rates of respiration were stimulated by addition of succinate, and further stimulated by adenosine diphosphate (ADP), indicating that the respiratory chain was functional and phosphate acceptor control remained intact. Analysis of variance indicated that brain homogenate respiration was significantly influenced by the level of corticosterone administered and the presence of ethanol in the vehicle THC, on the other hand, did not exert a singular effect on respiration but was found to interact significantly with the level of corticosterone and the presence of ethanol. With low levels of corticosterone, THC depressed respiration below that of animals receiving vehicle. With stress levels of corticosterone, THC stimulated tissue respiration above that of animals receiving vehicle. This dual effect of THC was even more pronounced when ethanol was added to the carrier vehicle. Observations demonstrate that the state of adrenal activity as well as the composition of injection vehicle can significantly influence an animal's metabolic reaction to cannabis. 12 references.

226765 Fuller, Ray W.; Perry, Kenneth W. Lilly Research Laboratoires, Eli Lilly and Company, Indianapolis, IN **Inability of an inhibitor of amine uptake (Lilly 110140) to block depletion of brain 5-hydroxytryptamine by L-dopa.** Journal of Pharmacy and Pharmacology (London). 27(8):618-620, 1975.

Rats and mice were studied to determine if 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenyl-propylamine hydrochloride (110140) altered 5-hydroxytryptamine (5-HT) release following L-dopa administration. L-Dopa reduced 5-HT concentrations by about half both in control mice and in 110140 treated mice. Treatment with 110140 alone produced a slight but statistically significant decrease in 5-hydroxyindoleacetic acid (5-HIAA) concentrations; this decrease is due to a compensatory decline in 5-HT turnover. L-Dopa evaluated 5-HIAA concentrations both in control mice and in 110140 pretreated mice. The effects of the same dose of L-dopa in rats were less pronounced than in mice, but again it was as effective in the 110140 pretreated group as in controls. 5-HT was significantly lowered in both groups, and 5-HIAA was significantly increased by L-dopa in both groups. The fact that 5-HIAA is elevated while 5-HT is lowered by L-dopa implies that the effect of L-dopa is to release 5-HT rather than to inhibit its synthesis. The finding that the effects of L-dopa are not blocked by an inhibitor of the amine uptake system on the neuronal membrane indicates that L-dopa is transported into the 5-HT neuron as the amino acid and is decarboxylated intraneuronally to dopamine, which displaces 5-HT from storage vesicles. All of these amines appear to require active transport into neurons via the membrane pump responsible for 5-HT reuptake, and the explanation for the blockade of their effects by 110140 is that their entry into the neuron is prevented. 8 references.

226766 Khalsa, J. H.; Davis, W. M. Department of Pharmacology, School of Pharmacy, University of Mississippi, MS 38677 **Effects of a dopamine beta-hydroxylase inhibitor on amphetamine-induced hyperactivity in rats.** Journal of Pharmacy and Pharmacology (London). 27(8):620-622, 1975.

The effects of a dopamine beta-hydroxylase inhibitor on amphetamine induced hyperactivity was examined in rats. The results indicate that hyperactivity induced in rats by 1 mg/kg of (+)-amphetamine, was significantly reduced by a single dose of 25 or 50mg/kg of 1-phenyl-3-(2-thiazolyl)-Z-thivrea (U-14,624). It was impossible to achieve a uniform suspension of U-14,624 to deliver an accurate and consistent dose. Furthermore, small pockets of unabsorbed drug were found in the peritoneal cavity at 48 h after U-14,624 in the methylcellulose vehicle, indicating a delayed and incompelte absorption of the drug from the site of injection. Results of the second activity study show that increased motility following the higher dose of (+)-amphetamine also was reduced significantly by U-14,624 if the interval between amphetamine and U-14,624 was 6 h, but not if the interval was 1 h. These data are consistent with the view that noradrenergic systems are essential to motility stimulation of amphetamine, either independently of dopaminergic systems or, as seems more likely, together with dopaminergic function. 18 references.

226826 Sofia, R. D.; Vassar, H. B. Department of Pharmacology and Toxicology, Wallace Laboratories, Half Acre Road, Cranbury, NJ 08512 **The effect of ergotamine and methysergide on serotonin metabolism in the rat brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 216(1):40-50, 1975.

The effects of ergotamine tartrate and methysergide maleate on serotonin (5-HT) metabolism in the rat brain were examined. Whole brain levels of 5-HT were markedly reduced in a dose related manner, with peak activity observed 30 minutes after I.P. administration and persisting through 4 hours after dosing. In addition, turnover rate of 5-HT was significantly increased. Pentylenetetrazol (PTZ) induced convulsions were not inhibited by either ergotamine or methysergide but each drug interacted with PTZ to induce lethality, which is suggestive evidence of central 5-HT antagonist activity. Regional distribution of 5-HT in the rat brain was altered by these drugs in such a way to suggest that neither was a universally acting central 5-HT antagonist. 19 references. (Author abstract)

226827 De Angelis, L.; Predominato, M.; Vertua, R. Institute of Pharmacology, University of Trieste, I-34100, Trieste, Italy **5-Hydroxytryptamine-14C and dexamphetamine-14C uptake by fundal sarcolemma preparations: effect of thermal and chemical alterations as indirect approach to the problem of the common receptor.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 216(1):51-56, 1975.

The effect of thermal and chemical alterations were examined as an approach to the common receptor problem in the rat. By submitting a sarcolemma preparation from gastric fundus to thermal and chemical (2 M urea) alterations, a significant decrease of the binding of labelled serotonin and dexamphetamine, 40% and 30% respectively, was observed. This finding suggests that the receptors for these two drugs contain a protein moiety, which undergoes a structural and functional modification upon the thermal or chemical procedure employed. The strictly similar behavior of the binding properties of serotonin and dexamphetamine gives a strong indirect support to the hypothesis of a common receptor for these two drugs. 10 references. (Author abstract)

226840 Sokol, Gerald H.; Greenblatt, David J.; Littman, Philip; Franke, Kate; Koch-Weser, Jan. Department of Radiation Medicine, Massachusetts General Hospital, Boston, MA 02114 **Chlordiazepoxide metabolism in mice following hepatic irradiation.** Pharmacology (Basel). 13(3):248-251, 1975.

The effect of hepatic irradiation upon the metabolism of chlordiazepoxide (Librium) in adult male mice was examined. Metabolic N-demethylation of chlordiazepoxide in irradiated mice was impaired when tested 3 days after irradiation. No such effect was observed in mice tested 3 weeks or 6 weeks after irradiation. It was concluded that hepatic irradiation produces short lived, reversible impairment of drug metabolizing function. 14 references. (Author abstract modified)

226849 Liu, Shean-Jan; Huang, Chian L.; Waters, I. W. Pharmacology Research Laboratories, VA Center, Wood, WI 53193 **Interactions of tricyclic antidepressants and barbiturates in barbiturate-tolerant and nontolerant rats.** Journal of Pharmacology and Experimental Therapeutics. 194(2):285-295, 1975.

The interactions of tricylic antidepressants and barbiturates were examined in barbiturate tolerant and nontolerant rats. Pretreatment of rats with tricyclic antidepressants, imipramine, desipramine, amitriptyline at two doses 20 minutes before administration of barbiturate markedly reduced the latent period of the response to barbital and prolonged the sleeping time induced by pentobarbital (PB) and barbital; effects were dose dependent. The effect of tricyclic antidepressants on PB hypnosis in PB tolerant and nontolerant rats was apparently not related to change in central nervous system (CNS) sensitivity to PB, since at the time of awakening there were no significant differences in the concentrations of unmetabolized PB in either the plasma or brain of tricyclic antidepressant treated animals as compared to controls. It is concluded that tricylcic antidepressants prolong PB sleeping time in PB tolerant and nontolerant rats by inhibiting its biotransformation in the liver. The action of tricyclic antidepressants to prolong the hypnotic action of barbital in normal rats is related to their direct effects of CNS sensitivity to barbital, but such effects are markedly diminished after animals become tolerant to barbital. 48 references. (Author abstract modified)

226850 Taylor, K. M.; Randall, P. K. Roche Research Insitute of Marine Pharmacology, P.O. Box 255, Dee Why, New South Wales, 2099, Australia **Depletion of S-adenosyl-L-methionine in mouse brain by antidepressive drugs.** Journal of Pharmacology and Experimental Therapeutics. 194(2):202-310, 1975.

A sensitive enzymatic isotopic method based on the methylation of histamine by histamine methyltransferase was used to measure the endogenous concentration of S-adenosyl-L-methionine in mouse brain. After a single dose of imipramine, DL-dopa, pargyline or d-amphetamine, brain S-adenosyl-L-methionine levels were 50% depleted after 1 hour, but had returned to normal values within 4 hours after drug treatment. A similar but long lasting depletion of S-adenosyl-L-methionine was obtained after chronic treatment with imipramine or after a single dose of cycloleucine, a drug that interferes with the synthesis of S-adenosyl-L-methionine from methionine. The rate of methylation of 3H-norepinephrine given by intraventricular injection suggested that the decreased levels of S-adenosyl-L-methionine after the administration of cycloleucine and after the chronic, but not the acute, administration of imipramine may interfere with the inactivation of norepinephrine in the mouse brain. These results indicate that decreased methylation may contribute to the neurochemical effects of antidepressive drugs. 24 references. (Author abstract)

226851 Carenzi, A.; Guidotti, A.; Revuelta, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC **Molecular mechanisms in the action of morphine and viminol (R2) on rat striatum.** Journal of Pharmacology and Experimental Therapuetics. 1994(2):311-318, 1975.

The molecular mechanisms in the action of morphine and viminal (R2) were examined on the rat striatum. Analgesic doses of morphine and viminol R2 increase the turnover rate of dopamine (DA) in rat striatum but fail to increase the striatal concentration of adenosine 3',5'-monophosphate (cAMP) or the affinity of tyrosine hydroxylase (TH) for the pteridine cofactor. When morphine is added to striatal homogenates, it changes neither the basal activity of adenylate cyclase nor the enzyme activation by DA. Similarly to morphine, haloperidol enhances th turnover rate of striatal DA, but unlike morphine it increases the affinity of TH for the pteridine cofactor and blocks the in vitro activation of striatal adenylate cyclase by DA. Results show that although (+)-amphetamine, haloperidol and morphine increase the turnover rate of striatal DA, each drug possesses a specific profile in its action on molecular mechanisms that control the function of striatal dopaminergic synapses. 38 references. (Author abstract modified)

226855 Branisteanu, Dimitrie D.; Volle, Robert L. Department of Pharmacology, University of Connecticut Health Center, Farmington, CT 06032 **Modification by lithium of transmitter release at the neuromuscular junction of the frog.** Journal of Pharmacology and Experimental Therapeutics. 194(2):362-372, 1975.

The effect of lithium (Li+) on transmitter release was examined at the frog neuromuscular junction. Complete or partial replacement of sodium (Na+) by Li+ resulted in a progressively developing increase in the amplitude and quantal content of end plate potentials of the frog neuromuscular junction. Analysis of frequency facilitation curves and estimations of the binomial parameters of release indicate that Li+ caused an increase in the probability of transmitter release. Li+ also caused a time dependent increase in the frequency of miniature end plate potentials. The responsiveness of the miniature end plate potentials to Li+ was depressed by elevated calcium Ca++— and enhanced by elevated potassium (K+). Collectively, the effects of Li+ on transmitter release can be attributed to the accumulation by the nerve terminals of Li+ resulting in an increased level of intracellular Ca++. 34 references. (Author abstract)

226856 Roth, Robert H.; Morgenroth, Victor H., III; Salzman, Phyllis M. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Tyrosine hydroxylase: allosteric activation induced by stimulation of central noradrenergic neurons.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 289(4):327-343, 1975.

The allosteric activation of tyrosine hydroxylase induced by stimulation of rat central noradrenergic neurons is reported. It is noted that electrical stimulation of the rat locus coeruleus causes about a 300% increase in the activity of the tyrosine hydroxylase prepared from the hippocampus on the stimulated side and assayed in the presence of subsaturating concentrations of tyrosine and pteridine cofactor. Addition of calcium cyclic-adenosine monophosphate (c-AMP) to soluble preparations of tyrosine hydroxylase isolated from the hippocampus produces a similar activation of tyrosine hydroxylase. The activation of tyrosine hydroxylase produced by calcium is reversed by addition of the calcium chelator, EGTA, while the activation produced by cAMP addition or by electrical stimulation of the locus coeruleus is unaffected by addition of EGTA to the assay medium. All treatment causes the enzyme to have an increased affinity for substrate and pteridine cofactor and a decreased affinity for the endproduct inhibitor, norepinephrine. Results are suggestive that the activation of tyrosine hydroxylase wwhich occurs during periods of increased impulse flow in noradrenergic neurons may be initiated by alterations in calcium fluxes or by changes in the steady state levels of cAMP which accompany neuronal depolarization. 34 references. (Author abstract modified)

226857 Mao, C. C.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Evidence for an involvement of GABA in the mediation of the cerebellar cGMP decrease and the anticonvulsant action of diazepam.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 289(4):369-378, 1975.

Evidence for an involvement of gamma-aminobutyric acid (GABA) in the mediation of the cerebellar 3',5'-cyclic guanosine monophosphate (cGMP) decrease and the anticonvulsant action of diazepam is presented. Subcutaneous injections of isoniazid or picrotoxin increase the cerebellar content of (cGMP) without changing the 3',5'-cyclic adenosine monophosphate (cAMP). Increase was dose dependent and the threshold for the cGMP increase was lower than that for convulsions. In cerebellum the increase of cGMP content elicited by isoniazid but not that caused by picrotoxin, was paralleled by a decrease of GABA content. Diazepam produced a dose dependent decrease of cerebellar cGMP concentration without changing cAMP or GABA content. Diazepam produced a dose dependent decrease of cerebellar cGMP concentration without changing cAMP or GABA content. Smaller doses of diazepam failed to decrease the basal cerebellar content of cGMP. However, this dose of diazepam antagonized the increase of cGMP produced by isoniazid but not that produced by picrotoxin. Higher doses of diazepam were necessary to block the increase of cerebellar cGMP elicited by picrotoxin. Low doses of diazepam antagonized the convulsions in 50% of the rats injected with isoniazid. The results suggest that diazepam may act in the CNS either by altering the disposition of endogenous GABA or by mimicking the action of GABA at specific synaptic receptors. 24 references. (Author abstract modified)

226858 Scatton, B.; Garret; C.; Julou, L. Laboratories de Recherches de la Societe Rhone-Poulenc, Vitry-sur-Seine, France **Acute and subacute effects of neuroleptics on dopamine synthesis and release in the rat striatum.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 289(4):419-434, 1975.

The effects of acute and subacute treatments with moderate doses of thioproperazine and haloperidol on dopamine synthesis and release were examined in rat striatal slices. Synthesis and release of dopamine were determined by measuring the rate of formation of 3H-H2O during the conversion of L-3,5-3H-tyrosine into 3H-Dopa and the accumulation of newly synthesized 3H-dopamine in striatal slices and their incubating medium. Possible effects of the treatments on tyrosine striatal levels or tyrosine specific activity were also investigated. Dopamine synthesis rate was markedly accelerated 2.5hrs after the acute injection of thioproperazine, but was equal to control levels 24 hrs later. Dopamine synthesis and release were still markedly increased 2.5hrs after the last injection of the subacute neuroleptic treatments when compared to controls, but these effects were less pronounced than those observed 2.5hrs after an acute injection of either drug. Dopamine synthesis and release were significantly decreased 24 hrs after the last injection of the subacute neuroleptic treatments when compared to controls. Two hypotheses are proposed to explain the changes in dopamine synthesis induced by repeated treatments with neuroleptics. 40 references. (Author abstract modified)

226865 Schnell, R. C.; Stoll, R. E.; Johnston, R. E.; Prosser, T. D.; Paolino, R. M.; Bousquet, W. F. Dept. of Pharmacology and Toxicology, School of Pharmacy and Pharmacal Science, Purdue University, West Lafayette, IN 47907 **Similarity in CNS sensitivity to hexobarbital in the rat and mouse as determined by an analytical, a pharmacokinetic, and an electroencephalographic measure.** Pharmacology (Basel). 13(1):20-26, 1975.

Sensitivity of the central nervous system (CNS) to the hypnotic effect of hexobarbital was assessed by analytical, pharmacokinetic, and electroencephalographic techniques in male and female rats and in mice of both sexes by the first two techniques. These experimentally and conceptually diverse measures yielded strikingly similar estimates of CNS sensitivity to hexobarbital which was independent of both species and sex, while well known species and sex (rat) differences in duration of response to hexobarbital were demonstrated. 12 references. (Author abstract)

226869 Meltzer, Herbert Y.; Daniels, Stephen; Fang, Victor S. Department of Psychiatry, University of Chicago School of Medicine, 950 E. 59th St., Chicago, IL 60637 **Clozapine increases rat serum prolactin levels.** Life Sciences (Oxford). 17(3):339-342, 1975.

The effects of clozapine on rat serum prolactin levels were examined. Clozapine markedly increased serum prolactin levels in male rats when injected intraperitoneally in doses of 5, 10, 50 and 100mg/kg. Serum prolactin levels after 5mg/kg clozapine were significantly less than in rats given 10, 50 and 100mg/kg which did not significantly differ from each other. Serum prolactin after 10mg/kg clozapine was significantly greater than after chlorpromazine, 5mg/kg and haloperidol, 0.5mg/kg. The increases in serum prolactin are attributed to clozapine's ability to produce dopamine blockade or to inhibit nerve impulse dopamine release, or both. The capacity of clozapine to affect brain serotonin and norepinephrine metabolism and its strong antichloinergic properties are probably not involved in its ability to increase serum prolactin. 29 references. (Author abstract modified)

226870 Perez-Cruet, Jorge; Thoa, Nguyen B.; Ng, Larry K. Y. Laboratory of Clinical Sciences, NIMH, Bethesda, MD **Acute effects of heroin and morphine on newly synthesized serotonin in rat brain.** Life Sciences (Oxford). 17(3):349-362, 1975.

The acute effects of heroin and morphine on newly synthesized serotonin in rat brain were examined. Heroin and morphine, in acute intraperitoneal doses produced significant increments in the formation of newly formed brain serotonin from tritiated (3H)-L-tryptophan to 3H-serotonin. Opiate analgesia, Straub tail sign and catatonia, were observed during the increase in the synthesis of serotonin. The transport of radiolabelled tryptophan into the rat brain was not increased by the acute injection of the opiates, but brain levels of 3H-serotonin and of its main metabolite, 5-hydroxyindoleacetic acid, were significantly elevated. These opiates do not interfere with the accumulation of serotonin or with the transport of its metabolite in serotonin or with the transport of its metabolite in serotonergic neurons after inhibition of monoamine oxidases with pargyline. An increase in the activity of tryptophan hydroxylases was more pronounced in the forebrain than in the brainstem. Stimulation of newly synthesized serotonin is probably mediated by an increase in tryptophan hydroxylase activity and not by an increase in the transport of tryptophan into the brain. 59 references. (Author atract)

226871 Thornton, Everard W.; Goudie, Andrew J.; Bithell, Victoria. Development of Psychology, University of Liverpool, Liverpool, England **The effects of neonatal 6-hydroxydopamine induced sympathectomy on response inhibition in extinction.** Life Sciences (Oxford). 17(3):363-368, 1975.

The effects of sympathectomy, induced by neonatal treatment with 6-hydroxydopamine (6-OHDA), on frustration was assessed by response inhibition in extinction following continuous free operant reward training. The results show a positive effect on behavior, specifically in terms of enhanced response rate during extinction in treated animals. Analysis of the results does not support a previous hypothesis for a deficit in the ability to inhibit responding. Though the results were consistent with the theory of equivalence of the aversive affective states of frustration and fear, the evidence for a definitive role of the peripheral nervous system in such states is confounded by changes in central catecholamines by neonatal 6-OHDA treatment. The results provide further evidence of the importance of catecholamines in affective behavior. 29 references. (Author abstract modified)

226873 Fernstrom, John D.; Hirsch, Madelyn J. Laboratory of Brain and Metabolism, Department of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Rapid repletion of brain serotonin in malnourished corn-fed rats following L-tryptophan injection.** Life Sciences (Oxford). 17(3):455-463, 1975.

The concentration of tryptophan in serum, and the levels of tryptophan, serotonin (5-HT), and 5-hydroxyindoleacetic acid (5-HIAA) in brain were examined in rats that consumed for 6 weeks a diet in which corn was the only source of protein. Single injections of L-tryptophan caused dose related increases in brain tryptophan, 5-HT, and 5-HIAA in corn fed animals. At each dose, brain tryptophan content rose to a proportionately greater extent in corn fed rats than in well nourished controls, even though serum tryptophan concentrations attained higher levels in controls. This difference reflects the greatly reduced serum concentrations in corn fed rats of other large neutral amino acids that compete with tryptophan for uptake into the brain (tyrosine, phenylalanine, leucine, isoleucine, and valine). The fact that tryptophan administration rapidly restores brain 5-hydroxyindole levels in corn fed animals suggests that the reductions in 5-HT and 5-HIAA levels associated with this type of malnutrition may be largely caused by inadequate availability of substrate. 25 references. (Author abstract modified)

226927 Vorne, M. S.; Puolakka, J. O.; Idanpaan-Heikkila, J. E. Department of Clinical Chemistry, Univ. of Oulu, 90220 Oulu 22, Finland **Diazepam, ethanol and drug metabolizing enzymes in rat liver.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 216(2):280-287, 1975.

The effect of diazepam and/or ethanol treatment of 7 days on the drug metabolizing enzymes in rat liver microsomes was studied. Diazepam decreased the metabolism rate of 3,4-benzpyrene by 38% and that of p-nitrobenzoic acid by 15%. Ethanol increased the metabolism rate of N-methylaniline by 15% and decreased the reduction of p-nitrobenzoic acid by 48%. Although diazepam alone had no inducing effect, its use with ethanol increased the cytochrome P-450 content (56%) and the rate of metabolism of N-methylaniline (44%) more than ethanol alone. The rate of metabolism of diazepam was not affected by any treatment. 41 references. (Author abstract)

226928 Gigon, P. L. Medizinisch-chemisches Institut, University of Berne, Berne, Switzerland **Biotransformation and biliary excretion of imipramine in rats under various experimental conditions.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 216(2):315-327, 1975.

The biotransformation and biliary excretion of imipramine was examined in rats. After intraperitoneal administration of 14C-imipramine to male rats, the percentage of the dose found in liver and determined as imipramine plus metabolites was 13-15% independently of whether a bile fistula had been inserted or not; 25% of this percentage was located in the hepatic microsomal fraction. The simultaneous administration of pentobarbital and/or diphenylhydantoin did not alter these findings. The metabolite pattern, however, was shifted in favor of unmetabolized imipramine. In male rats without bile fistula, the enterohepatic circulation had no effect on the amount and the metabolite pattern of imipramine plus metabolites excreted into bile. In female rats without bile fistula, the percentage of an identical imipramine dose was only 7%. The percentage of unmetabolized imipramine in liver was double that found in male rats. Simultaneous administration of

imipramine and pentobarbital at the same dosage as in male rats was lethal for female rats without bile fistula within 30 min. 8 references. (Author abstract modified)

226935 Black, Ira B. Department of Neurology, Cornell University, Medical Center, New York, NY 10021 **Increased tyrosine hydroxylase activity in frontal cortex and cerebellum after reserpine.** Brain Research (Amsterdam). 95(1):170-176, 1975.

A modification of an existing radiochemical tyrosine hydroxylase (T-OH) assay which allowed the measurement of enzyme activity in the cerebral cortex and cerebellum as well as the locus coeruleus was examined in the rat. After reserpine treatment, significant rises in enzyme activity occurred in the cerebral cortex, cerebellum and locus coerulus. However, the rates of increase for T-OH activity were similar for the forntal cortex and cerebellum but differed markedly from that of the locus coerulus. It is suggested that these differences may reflect the different factors governing enzyme turnover in perikarya and nerve terminals. 29 references.

227133 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, England **Neuropharmacological studies on D145 (1,3-dimethyl-5-aminoadamantan).** Psychopharmacologia (Berlin). 43(1):53-61, 1975.

The effects of D145 (1,3-dimethyl-5-aminonadamantan) and amantadine on dopaminergic mechanisms in the rat were investigated by use of pharmacological agents known to disrupt dopamine function, by placing electrolytic lesions in the dopamine containing areas of the extrapyramidal and mesolmbic systems and by the direct application to dopamine sensitive areas. The possible importance of 5-hydroxytryptamine to the dopamine effects was investigated using electrolytic lesions of the midbrain raphe nuclei. Both D145 and amantadine caused a stereotyped behavior characterised by periodic sniffing, repetitive limb movements and bitting, but the effect of amantadine was far more periodic. In addition D145, but not amantadine, caused marked hyperactivity. Both D145 and amantadine caused circling behavior in animals with asymmetric lesions of the medial raphe nucleus of unilateral lesions of the substantia nigra but the action of D145 was more intense. Bilateral electrolytic lesions placed in the extrapyramidal mesolimbia nuclei or the neuronal pathways supplying them showed D145 and amantadine to act in both areas although their action on the extrapyramidal system was most marked. Lesions placed in the medial and/or dorsal raphe nucleus indicated some involvement of 5-hydroxytryptamine with the actions of both D145 and amantadine. 19 references. (Author abstract modified)

227134 Zis, A. P.; Fibiger, H. C. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia **Neuroleptic-induced deficits in food and water regulation: similarities to the lateral hypothalamic syndrome.** Psychopharmacologia (Berlin). 43(1):63-68, 1975.

The role of central dopaminergic mechanisms in the regulation of food and water intake was assessed by examining the effects of haloperidol and pimozide on various measures of feeding and drinking in rats. Haloperidol or pimozide did not significantly affect 1 hr water intake in response to 24 hrs of water deprivation, nor did they influence 2 hr food intake after 24 hrs of food deprivation. Both pimozide and haloperidol significantly reduced drinking in response to injections of hypertonic saline. Animals pretreated with these drugs drank less than controls in the absence of food and drank less than controls when the water was adulterated with quinine. These drugs significantly reduced food intake in response to injections of insulin and attenuated amphetamine anorexia. These deficits are similar to those observed after electrolytic lesions of the lateral hypothalamus or after 6-hydroxydopamine lesions of the substantia nigra. The findings are consistent with the hypothesis that part of the lateral hypothalamic syndrome is the result of damage to the dopaminergic nigro striatal projection. The data suggest that the changes in feeding and drinkinginduced by haloperidol and pimozide reflect genuine homeostatic deficits rather than a neuroleptic induced motor dysfunction. 29 references. (Author abstract modified)

227139 Trenchard, Ann; Turner, P.; Pare, C. M. B.; Hills, M. Department of Clinical Pharmacology, St. Bartholomew's Hospital, London **The effects of protriptyline and clomipramine in vitro on the uptake of 5-hydroxytryptamine and dopamine in human platelet-rich plasma.** Psychopharmacologia (Berlin). 43(1):89-93, 1975.

The effects of protriptyline and clomipramine were studied in vitro on the uptake of 5-hydroxytryptamine (5-HT) and dopamine (DA) uptake in human platelet rich plasma. It was found that the tertiary amine, clomipramine, was a more potent inhibitor of 5-HT uptake than the secondary amine, protriptyline. The activity of both compounds was competitive, but it was thought unlikely that they acted through tryptamine receptor sites as methysergide had very little effect on 5-HT uptake. Neither tricyclic antidepressant had any marked effect on DA uptake. 15 references. (Author abstract)

227343 Antelman, Seymour M.; Szechtman, Henry. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15260 **Tail pinch induces eating in sated rats which appears to depend on nigrostriatal dopamine.** Science. 189(4204):731-733, 1975.

The respective roles of norepinephrine and dopamine were examined in relation to tail pinch induced eating in rats. Mild tail pinch reliably induced eating, gnawing or licking behavior in all animals tested, with eating the predominant response by far. Pharmacological analysis of the involvement of the brain catecholamines in tail pinch behavior suggests that it is critically dependent on the nigrostriatal dopamine system. 13 references. (Author abstract)

227384 Reiter, Lawrence W.; Talens, Gloria M.; Woolley, Dorothy E. National Environmental Research Center, Environmental Protection Agency Technical Center, Research Triangle Park, NC **Parathion administration in the monkey: time course of inhibition and recovery of blood cholinesterases and visual discrimination performances.** Toxicology and Applied Pharmacology. 33(1):1-13, 1975.

The effects of parathion (O,O-diethyl O-p-nitrophenyl phosphorothionate) administration on activities of acetylcholinesterase (AChE) in blood and pseudocholinesterase (ChE) in plasma were studied in bonnet (Macaca radiata) and rhesus (M. mulatta) monkeys. In addition, the effects of parathion administration on performance of learned visual discrimination tasks were studied in rhesus monkeys. Peak inhibition of AChE and ChE occurred about 6 hr after administration of 0.5, 1.0, and 2.0mg/kg parathion po. The degree of peak inhibition was greater for ChE than for AChE, was dose related for both enzymes, and was of about the same magnitude in both species, even though control values for AChE and ChE differed in the two species. It is concluded that reversal of blood AChE and ChE inhibition after parathion administration occurred more rapidly in mon-

key than in man but required more time in monkey than in mouse. It was observed that scopolamine and methyl scopolamine also blocked visual discrimination performance. 22 references. (Author abstract modified)

227387 Dietz, D. D.; Sellinger, O. Z. Department of Environmental and Industrial Health, Mental Health Research Insitute, University of Michigan, Ann Arbor, MI **Differential regional effects of the convulsant methionine sulfoximine on serotonin turnover in the rat brain.** Tosicology and Applied Pharmacology. 33(1):162-163, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williamsburg, Virginia, in March 1973, a paper was presented in which the differential regional effects of the convulsant methionine sulfoximine MSO on serotonin (5-HT) turnover in the rat brain were reported. The type A monoamine oxidase inhibitor clorgyline (N-methyl-N-propargyl-3(2,4-dichlorophenoxy) propylamine was given to adult male rats in a dose of 2mg/kg iv, 3 hr after a subconvulsant dose of mso or saline ip. The rats were sacrificed at 0 time, 10 min, and 2 hr after clorgyline. 5 HT and its deaminated metabolite, 5-hydroxyindoleacetic acid (5-HIAA) were fluorimetrically determined in seven neuroanatomical regions of the rat brain after 2 hr and in the striatum, cerebral cortex, brainstem, and midbrain at the early time points. Results show that MSO antagonized the clorgyline induced buildup of 5-HT in the cerebral cortex and the brainstem, while it was without effect in the midbrain. Results suggest that MSO alters turnover rate of 5-HT differentially in various areas of discrete rat brain. (Journal abstract modified)

227389 Catravas, J. D.; Waters, I. W.; Burdock, G. A.; Davis, W. M. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS **Haloperidol and propranolol in the treatment of acute amphetamine intoxication in the dog.** Toxicology and Applied Pharmacology. 33(1):184-185, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williamsburg, Virginia, in March 1973, a paper was presented in which the effects were reported of haloperidol and propranolol in the treatment of acute amphetamine intoxication in the dog. A lethal intravenous dose of d-amphetamine sulfate was administered to unanesthetized mongrel dogs, and six stages of toxicity were observed. Amphetamine produced increases in body temperature, systemic arterial systolic and diastolic pressures, left ventricular pressure, mean right atrial pressure, heartrate, cardiac output, stroke volume, total peripheral resistance, oxygen uptake, respiratory rate, tidal volume, minute volume, blood lactate and pyruvate, plasma urea nitrogen, plasma glutamic oxaloacetic transaminase and glutaminc pyruvic transaminase, and a decrease in plasma glucose. The mean survival time was 2 hr. The lethal actions of amphetamine were challenged in a second group of conscious dogs by the intravenous administration of 1 mg/kg haloperidol or 0.5-6.0mg/kg propranolol at the beginning of stage two. All haloperidol treated animals survived and their physiological variables remained normal; they were kept under observation for an additional 48 hr. Propranolol showed no appreciable protection and did not change the mean amphetamine survival time. The results indicate a definite protective role of haloperidol against amphetamine lethality and allow an optimistic view for its clinical use in acute intoxication. (Journal abstract modified)

227390 Waters, I. W.; Liu, S. J. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS **Interactions of tricyclic antidepressants and pentobarbital in pentobarbital-tolerant and nontolerant rats.** Toxicology andApplied Pharmacology. 33(1):186-187, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williamsburg, Virginia, in March 1973, a paper was presented in which they interactions of tricyclic antidepressants and pentobarbital in pentobarbital tolerant and nontolerant rats were reported. Pretreatreament of rats with imipramine (IP), desipramine (DI), amitriptyline (AT), or nortriptyline (NT) prior to pentobarbital prolonged pentobarbital sleep time. The effect was dose dependent. Rats treated with DI showed decreases in the rate of disappearance of (14C)pentobarbital from both brain and plasma, although the concentration of (14C)pentobarbital in these two tissues was not different from controls at return of righting reflex. Pentobarbtial tolerant rats pretreated with either IP, DI, AT, or NT 20 min prior to pentobarbital slept longer than pentobarbital-tolerant controls, although at awakening, brain and plasma concentrations of (14C)pentobarbital in the treated animals were not different from control values. Addition of each of the tricyclic drugs to an in vitro hepatic microsomal enzyme system showed competitive inhibition of pentobarbital metabolism. Neither of the tricylcic drugs enhanced significantly the development of tolerance to pentobarbital although the combination of pentobarbtial and DI stimulated pentobarbital hydroxylase activity. (Journal abstract modified)

227400 Snyder, Solomon H.; Chang, Ken J.; Kuhar, Michael J.; Yamamura, Henry I. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Biochemical identification of the mammalian muscarinic cholinergic receptor.** Federation Proceedings. 34(10:1915-1921, 1975.

The biochemical identification of the mammalian muscarinic cholinergic receptor is described. The muscarinic cholinergic antagonist 3-quinuclidinyl benzilate (QNB) binds avidly but reversibly to the muscarinic cholinergic receptor of mammalian brain and peripheral tissues. (3H)QNB binding provides a simple, sensitive, specific assay for the muscarinic cholinergic receptor binding. Inhibition of (3H)QNB binding to homogenates of brain and guinea-pig ileum by muscarinic drugs correlates with their pharmacologic potencies, while nicotinic agents and noncholinergic drugs have negligible affinity. The regional distribution of (3H)QNB binding throughout rat and monkey brain parallels to a major extent other cholinergic markers, suggesting that the majority of cholinergic synapses in the brain are muscarinic. (3H)QNB accumulation in various brain regions after intravenous injection provides a means of labeling the muscarinic receptor in vivo. By labeling the receptor in vivo, autoradiographic studies under the light microscope have been performed to visualize the muscarinic receptor. 66 references. (Author abstract)

227635 Billewicz-Stankiewicz, Jaroslaw; Gorny, Dionizy; Zajaczkowska, Maria. Zaklad Patologii Ogolnej i Doswiadczalnej AM, 20-090 Lublin, Jaczewskiego 8, Poland **The effects of adrenaline, reserpine, and atropine on acetylcholine content of the brain and peripheral ganglia in stress.** Acta Physiologica Polonica (Warszawa). 26(3):289-297, 1975.

The effects of adrenaline, reserpine and atropine on acetylcholine (ACh) content in the cerebral cortex and brainstem and in the gastric tissues were investigated in rats at rest and during stress induced by forced swimming. Adrenaline administered intraperitoneally twice at an interval of 2 hours in doses of 0.1mg/kg and then subcutaneously in a dose 0.5mg/kg increased acetylcholine content in the cerebral cortex of rest-

ing and in the gastric tissues of resting and swimming rats. Reserpine in doses of 3 mg/kg given 48, 24 and 7 hours before the experiment caused a significant rise in ACh content in the cerebral cortex of resting rats and in the brainstem during stress. Atropine given in a dose of 6 mg/kg at 8 hour intervals during 2 days caused a significant fall in ACh level in the cerebral cortex and brainstem of resting rats, in the cortex of swimming animals, as well as a considerable rise in the gastric tissues of swimming rats. 16 references. (Author abstract)

227692 Christian, S. T.; McClain, L. D.; Morin, R. D.; Benington, F. Neurosciences Program, University of Alabama Medical Center, University Station, Birmingham, AL 35294 **Blockage of LSD binding at its high affinity site on synaptosomal membranes by 1-methyl-1,2,5,6-tetrahydropyridine-N,N-diethyl-carboxamide.** . Experientia (Basel). 31(8):910-911, 1975.

Studies were undertaken to obtain molecular evidence for the blockage of lysergic acid diethylamide (LSD) binding by 1-methyl-1,2,5,6-tetrahydropyridine-N,N-diethylcarboxamide (THPC). Equilibrium dialysis was used to quantify the binding of LSD to its high affinity binding site on synaptosomal membranes from rat brain. Various concentrations of tritiated LSD were dialyzed against synaptic membrane preparations. Lysed rather than intact synaptosomes were used to preclude the possibility of confusing uptake with binding. Results indicate that the binding of LSD to its high affinity site on the synaptosomal membrane is completely blocked by the THC added to the dialysis medium. THPC is only one of a very few compounds that have been documented as blockers of the behavioral effects of LSD. These findings confirm this blockade at the receptor level. 8 references.

227694 Marcy, R.; Quermonne, M. A. Dept. of Pharmacology, Univ. of Caen, 1, rue Vaubenard, F-14032, Caen Cedex, France **Benzodiazepines: a comparison of their effects in mice on the magnitude of the palmar skin conductivity response and on pentylenetrazole-induced seizures.** Experientia (Basel). 31(8):954-955, 1975.

The effects of 13 benzodiazepines on the magnitude of palmar skin conductivity response (PSCR) and on pentylenetetrazole induced seizures (APIS) were compared in mice. Effects of phenobarbital and meprobamate were also examined. The various compounds showed greatly differing potencies in the two tests, suggesting that APIS and PSCR are likely to indicate two different pharmacological actions. Anticonvulsant benzodiazepines (flunitrazepam and clonazepam) reveal an activity ratio (APIS/PSCR) of seven. However, sedative benzodiapines present an activity ratio which is either around one, like meprobamate and phenobarbital, or close to 1.5. 6 references.

227696 Vorne, Martti; Idanpaan-Heikkila, Juhana. Dept. of Pharmacology, University of Oulu, Oulu, Finland **Inhibition of drug metabolizing enzymes by diazepam in rat liver.** Experientia (Basel). 31(8):962-963, 1975.

The effect on rat hepatic drug metabolizing activity of oral dosing of diazepam was determined in vitro. Diazepam had no significant effect on the content of cytochrome P-450 or N-demethylation on methylaniline. On the other hand, the oxidation of hexobarbital and reduction of p-nitrobenzoic acid were significantly inhibited by diazepam. Diazepam had no effect on its own metabolism. The effects of diazepam on drug metabolism differed entirely from those of phenobarbital, but they were to some extent similar to those of the polycyclic hydrocarbon 3,4-benzpyrene. 20 references.

227701 Colasanti, Brenda; Kirchman, Aviva; Khazan, Naim. Dept. of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Changes in the electroencephalogram and REM sleep time during morphine abstinence in pellet-implanted rats.** Research Communications in Chemical Pathology and Pharmacology. 12(1):163-172, 1975.

Changes in the electroencephalogram (EEG) and rapid eye movement (REM) sleep time were studied in rats prepared with permanent electrodes for recording the EEG and the electromyogram (EMG) and made dependent on morphine by the subcutaneous implantation of pellets of the drug. Abstinence was then precipitated by removal of the pellets 72 hours later. Results indicate that the evaluation of continuous EEG and EMG recordings showed a maximal reduction in the amount of REM sleep and a decline in its EEG voltage output during the first day after pellet removal. Both the duration of REM sleep and its mean integrated EEG voltage returned to the baseline levels by the second day of abstinence. A significant but short-term rebound subsequently followed and was accompanied by a trend toward elevation of the mean EEG voltage. It is suggested that these changes are reminiscent of similar findings in rats withdrawn from morphine administered intravenously (Khazan and Colasanti, 1971, 1972). The smaller magnitude of changes in rats treated with morphine pellets, however, may suggest a lower degree of drug dependence. 14 references. (Author abstract)

227712 Bender, D. A. Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London WlP 5PR, England **Serum-aminoacids and brain tryptophan uptake.** Lancet (London). 2(7928):278-279, 1975.

The effects of chlorpromazine on brain serotonin metabolism in rats are reported to demonstrate changes in brain tryptophan uptake and serotonin synthesis correlated with changes in serum diffusible tryptophan and reduction in diffusible tryptophan. Observations support prior findings indicating that it is the concentration of freely diffusible tryptophan rather the total serum tryptophan concentration that is important in controlling tryptophan uptake into the brain. It appears that both diffusible tryptophan concentration and the concentrations of competing amino acids are important as determinants of the rate of tryptophan uptake into the brain, and hence of serotonin synthesis. 7 references.

227774 Hughes, John. Marischal College, University of Aberdeen, Aberdeen AB9 1AS, Scotland **Isolation of an endogenous compound from the brain with pharmacological properties similar to morphine.** Brain Research (Amsterdam). 88(2):295-308, 1975.

An investigation was carried out to test the hypothesis that the brain contains a substance that functions as an endogenous mediator at central morphine receptor sites. The extraction and purification of a low molecular weight substance are described. This substance inhibits neurally evoked contractions of the mouse vas deferens and guinea-pig myenteric plexus. The inhibitory action of this substance was antagonized by the three narcotic antagonists naloxone, naltrexone and MR-1302 at nanomolar concentrations. The narcotic antagonists alone had no effect on the assay tissues. The morphine like substance was unevenly distributed in the brain. No activity could be detected in extracts of cerebellum, liver or lung. It is suggested that the compound isolated in this investigation forms part of a central pain suppressive system and may also have a wider neurochemical role in the brain. 15 references. (Author abstract modified)

227777 Roizen, M.; Thoa, N. B.; Moss, J.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Inhibition by halothane of exocytotic release of norepinephrine from guinea-pig vas deferens. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 1 p.

In a study of the mechanisms whereby halothane decreases plama levels of catecholamines, aeration with 1% or 2% halothane strikingly decreased spontaneous and nerve stimulation (NS) induced release of norepinephrine (NE) from the isolated phenoxybenzamine treated guinea-pig vas deferens. This was not due to ganglionic blockade since hexamethonium did not alter the stimulation induced release of NE nor the effects of halothane. Halothane did not proportionally decrease release of dopamine-beta-hydroxylase (DBH). During stimulation, NE was released mainly from the particulate fraction and halothane diminished the decrease in this fraction seen after NS. Release of NE and DBH by veratridine, which stimulates exocytosis, is also inhibited by halothane, but the diminution in release of NE is greater than that of DBH. Elevated levels of calcium do not reverse the effects of halothane. Release of NE by tyramine, which does not release DBH, is also prevented by halothane, but the anesthetic agent has no effect on the action of reserpine in releasing NE. Results suggest that halothane increases the ability of vesicles to bind NE in a form which is unavailable for release by exocytosis. (Author abstract modified)

227783 Fuentes, Jose A.; Neff, Norton H. Lab. of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Monoamine oxidases of the rat cardiovascular system. (Unpublished paper).** Washington DC, NIMH, 1975. 1 p.

The monoamine oxidases (MAO) of the rat cardiovascular system were foundto have different characteristics that those reported for rat brain and liver. MAO of most tissues have been differentiated into a type A and a type B enzyme. Type A enzyme deaminates norepinephrine (NE) and serotonin (5HT) and is inhibited by low concentrations of clorgyline, while type B deaminates 2-phenylethylamine (PEA) and it is inhibited by low concentrations of pargyline. Contrary to the results reported for the rat brain and liver, clorgyline and pargyline did not differentially inhibit the deamination of NE, 5HT or PEA when studied in the rat heart and mesenteric artery in vitro. Deamination of both NE and 5HT was almost completely blocked by both drugs, but PEA deamination was only completely blocked in the presence of semicarbazide. A similar blockade of enzyme activity was observed when the inhibitors were injected intravenously. (Author abstract modified)

227996 Costentin, J.; Protais, P.; Schwartz, J. C. Laboratoire de Pharmacodynamie et Physiologie, UER de Medecine-Pharmacie, 49 Rue Maulevrier, 76 Rouen, France **Rapid and dissociated changes in sensitivities of different dopamine receptors in mouse brain.** Nature (London). 257(5525):405-407, 1975.

In a study of changes in sensitivities of different dopamine receptors in mouse brain, it was observed that the sensitivity of dopamine receptors involved in thermoregulation and in a particular motor behavior can be rapidly altered after a single administration of an agonist (apomorphine) or an antagonist (haloperidol), respectively. Whereas dopamine receptors controlling thermoregulation are easily desensitized and do not develop supersensitivity, the reverse is true for those implicated in the motor behavior. The state of modified sensitivity had approximately the same duration after hypersensitization of haloperidol or desensitization by apomorphine. The easy desensitization of dopamine receptors involved in thermoregulation contrasts with their inability to exhibit hypersensitivity, although the opposite characterized those mediating climbing behavior, which could be hypersensitized but not desensitized. 16 references.

228032 Oleshansky, M. A.; Neff, N. H. Laboratory of Preliniical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **In vivo activation of rat pineal cAMP phosphodiesterase by isoproterenol. (Unpublished paper).** Washington, DC, NIMH, 1975. 1 p.

An in vivo study of activation of rat pineal cyclic adenosine monophosphate (cAMP) phosophodiesterase (PDE) is reported. It was found that l-isopropranolol (5mg/kg) treatment increased low kinetic activity PDE of pineal by 40% within one hour and the activity returned to normal within 5 hours. Activation was accompanied by a change of maximum velocity. Prior treatment of rats with propranolol blocked the increase of PDE activity while treatment with phentolamine did not, demonstrating modulation of enzyme activity through a beta-adrenergic receptor. Activity was apparently induced at postsynaptic sites, as PDE could still be activated after bilateral superior cervical ganglionectomy. Pretreatment of rats with cycloheximide prevented the response to isoproternol, indicating that protein synthesis was required. Treatment with aminophylline, a phosphodiesterase inhibitor, produced a small but significant increase of PDE activity. Aminophylline in combination with 1-isoproterenol below the threshold for PDE activation resulted in greater activity than with aminophylline alone. (Author abstract modified)

228050 Pycock, Chris; Anlezark, Gill. Dept. of Neurology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF **LSD and dopamine receptors.** Nature (London). 257(5521):69-70, 1975.

Studies are reported which attempted to replicate the findings of Pieri et al. of a circling behavior response to lysergic acid diethylamide (LSD) in rats with unilateral chemical lesions of the ascending medial forebrain bundle. Experiments in similar animal models produced apormorphine like (contraversive) circling behavior in only 40-50% of animals tested, and then only at very high drug levels. In the dose range 0.025-0.2mg/kg, LSD induced neither turing behavior or postural asymmetries nor significantly modified apomorphine or amphetamine induced circling. Apomorphine was at least 10 times more potent than LSD in blocking the clonic phase of audiogenic seizure in 50% of animals. 7 references.

228051 Pieri, L.; Pieri, M.; Haefely, W. F. Hoffman-La Roche & Co., Ltd., 4002 Basel, Switzerland **/LSD and dopamine receptors - Pieri reply./** Pieri et al. reply. Nature (London). 257(5521):70, 1975.

Pycock and Anlezark's failure to confirm prior findings of a circling behavior in response to lysergic acid diethylamide (LSD) is discussed and attributed to the use of a different animal species and a different lesion. Data suggest that LSD is slightly more potent than apomorphine as a striatal dopamine receptor agonist. 7 references.

228493 Zimmer, Louis John, II. University of Arizona **Some aspects of the roles of isoproterenol, angiotensin and the peripheral nervous system in thirst. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-19614 HC$13.50 MF$5.00 63 p.

Some aspects of the roles of isoproterenol, angiotensin and the peripheral nervous system in thirst were examined to test

earlier findings from an angiotensin antagonist experiment by changing the isoproterenol to a smaller dose infused intravenously. Results support earlier findings that the analog inhibited angiotension-II, but not isoproterenol, induced intake. In addition, to test the possibility that isoproterenol, induced hypotension needs to be maintained for long time periods to become effective when the kidneys are not present, a second injection of the drug was given 4 hr after the first. Bilaterally nephrectomized rats did not respond, while sham operated Ss did, but only to the first injection. Since the kidneys must be present for isoproterenol to induce thirst, but the renin released by the kidney is not necessary, other renal factors were explored by removing some of the renal innervation by spinal transection. Transection reduced the response of isoproterenol injection, but did not interfere with drinking produced by angiotension. Finally, observations that, since polyethylene glycol also reduces plasma volume as it produces thirst, the possibility that the same mechanism may be operative in controlling antidiuretic hormone (ADH) release and water intake was tested, without significant results. (Journal abstract modified)

228546 Arushanyan, Ye. B.; Belozertsev, Yu. A.; Ayvazov, K. G. Chitinskogo meditsinskogo instituta, U.S.S.R. **/The effect of d,1-amphetamine on the reaction of cortical neurons evoked by stimulation of mesodiencephalic structures./** Vliyaniye fenamina na reaktsii kortikal'nykh neyronov vyzvannyye razdrazheniyem mezodientsefal'nykh struktur. Farmakologiya i toksikologiya (Moskva). 38(4):389-392, 1975.

The effect of d,1-amphetamine on the reaction of cortical neurons evoked by stimulation of various parts of the mesodiencephalic activating system was investigated in 32 cats. Intravenous amphetamine in doses of 1-3mg/kg caused an increase in the number of responding units and a modification of the structure of the response and reaction intensity from the somatosensory cortex neurons following mesencephalic reticular formation stimulation. Phasic reactions were weakened and tonic reactions from the lateral hypothalamus were intensified and accompanied by a rise of nonreactive neurons. It is concluded that the action of amphetamine on the cortex depends not only upon mobilization of the brainstem reticular formation, but also on both greater reticular/hypothalamic interaction and direct excitation of the hypothalamic centers. 10 references. (Journal abstract modified)

228548 Korolenko, T. A.; Tsilli, Ye. I. Tsentral'naya nauchno-issledovatel'skaya laboratoriya, Novosibirskogo meditsinskogo instituta, Novosibirsk, U.S.S.R. **/The action of chlorpromazine on the permeability of the brain and liver lysosomes of rats in a state of hypoxia./** Vliyaniye aminazina na pronitsayemost' membran lizosom mozga i pecheni krys, nakhodyashchikhsya v sostoyanii gipoksii. Farmakologiya i toksikologiya (Moskva). 38(4):397-399, 1975.

The effect of chlorpromazine on the permeability of the cerebral membrane and liver lysosomes was investigated in 80 rats in a state of hypoxia. Hypoxia was induced by ether injections which restricted venous flow. The anemic hypoxia lasted for one hour following and did not change the permeability of either the cerebral membrane or the liver lysosomes. Chlorpromazine administration in doses of 30 mg/kg produced solubilization of the brain acid phosphatase. 12 references. (Journal abstract modified)

228550 Olsner, V.; Fischer, G.-D.; Staib, A. G.; von Shnartzenfeld, I. Institute Pharmacology and Toxicology, Medical Academy Karus", Dresden, East Germany **/Synthesis, release and distribution of acetylcholine in the brain of rats under the influence of cholinergic agents./** Sintez, osvobozhdeniye i raspredeleniye atsetilkholina v mozge krysy pod kholinergicheskim vozdeystviyem. Farmakologiya i toksikologiya (Moskva). 38(4):406-411, 1975.

The effects of scopolamine and arecoline on synthesis, release and distribution of acetylcholine in the brain were investigated in Wistar rats. The cholinergic agents were injected intramuscularly in doses of 1mg/kg. Acetylcholine distribution was determined biologically; acetylcholine liberation was determined by Scherber's push/pull technique. Both scopolamine and arecoline raised the content of acetylcholine synthesis in the cerebral tissue. Scopolamine increased acetylcholine release in all areas of the brain; arecoline increased release in the subcortical regions only. Further study of possible mechanisms of cholinergic agent action is recommended. 23 references. (Journal abstract modified)

228551 Arefolov, V. A.; Panasyuk, L. V. Laboratoriya farmakologii nervnoy sistemy, Instituta framakologii AMN SSSR, Moscow **/The capacity of adrenergic nerves to accumulate exogenous norepinephrine under the influence of some pharmacological agents./** Sposobnost' adrenergicheskikh nervov nakaplivat' ekzogennyy noradrenalin pri nekotorykh farmakologicheskikh vozdeystviyakh. Farmakologiya i toksikologiya (Moskva). 38(4):411-415, 1975.

The effect of antidepressants and the cholinolytic spasmolytin on the ability of the adrenergic nerves to accumulate exogenous norepinephrine (NE) was investigated in rats. NE content in the tissue and in the adrenergic nerves of the vas deferens was measured by spectrofluorometry and quantitative fluorescent histochemistry. Phthoracizine, imipramine and spasmolytin inhibited accumulation of exogenous NE, if the mediator was present in the extraneuronal medium in a concentration of 0.5microgram/ml. When the neurotransmitter was introduced into the medium in higher concentrations of .01mg/ml the antidepressants and spasmolytin lost their inhibitory affect. Correlations of spectrofluorometric and quantitative fluorescent histochemical findings were observed when the tissue contained less than 50% of the total NE reserves. 7 references. (Journal abstract modified)

228552 Komendantova, M. V.; Aleksandrova, G. M. Moskovskogo meditsinskogo stomatologicheskogo instituta im. N. A. Semaskho, Moscow **/On the mechanisms of action of aminopyrine./** O mekhanizme deystviya amidopirina. Farmakologiya i toksikologiya (Moskva). 38(4):415-419, 1975.

The effect of aminopyrine on bioelectrical reactions was investigated in unanesthetized cats. Aminopyrine (5-30mg/kg) had the following effects: 1) it increased the amplitude of an evoked potential of the somatosensory cortex and of the specific transmitting nucleus of the thalamus upon stimulation of the radial nerve; 2) it significantly lengthened the regeneration period of the neuron system excitability during paired stimulation; 3) it increased the number of high frequency oscillations and the amplitude of interzonal response in the cortical neuron system; 4) it lengthened the recovery period of neuron system excitability during paired stimulation. 20 references. (Journal abstract modified)

228553 Chichkanov, G. G. Laboratoriya farmakologii serdechno-sosudistoy sistemy, Instituta farmakologii AMN SSSR, Moscow **/The effect of diazepam and trifluoperazine on blood supply and cardiac activity./** Vliyaniye diazepama i triftazina na krovosnabzheniye i deyatel'nost' serdtsa. Farmakologiya i toksikologiya (Moskva). 38(4):423-427, 1975.

The effect of diazepam and trifluoperazine on blood supply and cardiac activity was investigated in anesthetized cats. Both diazepam and trifluoperazine produced hypotension and depressed the toncity of the coronary and renal vessels. Diazepam injections also caused bradycardia, a decrease in the maximum acceleration of the blood flow in the aorta; a decrease in cardiac output, an increase in systole, a decrease in coronary circulation rate and in decrease in oxygen uptake by the heart. Trifluoperazine augmented the blood outflow from the coronary sinus and increased oxygen uptake by the myocardium. Five to 10 minutes following trifluoperazine injection, tachycardia was produced and an intensification of myocardium contractility and cardiac output also occurred. 15 references. (Journal abstract modified)

229033 Huy, N. D.; Gailis, L.; Cote, G.; Roy, P. E. Centre de Recherche, Institut de Cardiologie de Quebec 2725, Chemin Ste-Foy, Sainte-Foy, Quebec, Canada G1V4G5 **Effects of chronic administration of delta 9-transtetrahydrocannabinol (delta9-THC) in guinea-pigs.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):284-289, 1975.

In a study of effects of chronic administration of delta 9-transtetrahydrocannabinol (delta9-THC), guinea-pigs were divided into three groups: 1) absolute control, 2) solvent control (tween 4%), and 3) delta9-THC group (3mg/kg). The selected dose of delta9-THC corresponds to the minimum amount producing physiological effects in acute administration and was given for 6 months at the rate of five injections per week. Results showed that THC produced no changes on these parameters: serum glucose, urea nitrogen, total proteins, magnesium, calcium, sodium and potassium. However, the fatty acids and alpha-1 globulin were significantly decreased. These was a significant increase in gamma globulin. The bodyweight of delta9-THC treated animals was lower than that of the two controls. Delta9-THC decreased the relative weight of liver and spleen; however, it did not significantly affect the relative weight of heart, adrenals, and kidneys. Similarly, the morphological examinations showed no alteration in these tissues, except in the liver tissue, where a perturbation of the autodigestion of glycogen was noted. Findings suggest that the toxic effect of the drug is caused by its accummulation in the liver, which inhibits certain liver enzymatic systems. 17 references. (Author abstract modified)

229035 Laurent, B.; Roy, P. E. Dept. of Experimental Medicine, Sainte-foy, Quebec, Canada G1V4G5 **Alteration of membrane integrity of delta1-tetrahydrocannabinol.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):261-266, 1975.

The incorporation of delta1-tetrahydrocannabinol (THC) into membranes is reported and biochemical proofs of its action in vitro are presented. THC was found to be a potent inhibitory of some membrane bound enzymes, such as magnesium adenosine triphosphatase (Mg-ATPase), sodium potassium adenosine triphosphatase (Na-K-ATPase) and acetylcholinesterase. At a given concentration, the degree of inhibition varied for each enzyme; the inhibition was more pronounced for the enzymes that are parts of the membranes. As the kinetic parameters of these enzymes are functions of the membrane composition and organization, these parameters were studied in vitro in the presence of THC. Although the Mg-ATPase was inhibited by THC, there was no change in the allosteric behavior of the enzyme. The Na-K-ATPase and acetylcholinesterase had a different allosteric behavior as compared to controls; these modifications were like the alterations caused by the decrease in membrane fluidity. Results suggest that THC is incorporated in the membranes and causes alterations in the physical organization of the membranes. 9 references. (Author abstract modified)

229041 Honecker, H. Institut fur Neurophyschopharmakologie der Freien Universitat Berlin, 1 Berlin 19, Ulmenallee 30, Germany **Studies on the CNS-availability of amphetamine from amphetaminil.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):121-128, 1975.

The biotransformation of amphetaminil to amphetamine was confirmed using 3H-labeled and 14C-labeled amphetaminil. The metabolites were isolated, identified and quantified from blood, brain, adipose tissue and urine of rats. Findings show that the intact molecule of amphetaminil passes into the circulation only to a very small extent. The time spent by the amphetaminil in the alimentary canal does not appear to be a critical factor in the stability and degredation of this substance. The proportion of unchanged amphetaminil represents no more than 2% of the total radioactivity in the blood. The amphetamine, which results from the cleavage of amphetaminil, enters the central nervous system and is excreted in the urine after hydroxylation and glucuronidation. The other cleavage product, benzaldehyde, seems to be rapidly converted into hippuric acid, which is excreted. Amphetaminil is enriched in adipose issue, especially after intraperitoneal injection; this fraction will be cleaved upon reentering the blood, however, and it can only enter the brain as amphetamine. 13 references. (Author abstract modified)

229068 Kato, Nobukatsu; Murase, Yoshinori. Dept. of Psychiatry and Neurology, Kyoto Prefectural University of Medicine, Kyoto, Japan **A histochemical study on the central effect of monoamine precursors.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 29(2):189-195, 1975.

A histochemical investigation of the central monoamine neurons after the administration of monoamine precursors and peripheral decarboxylase inhibitors in experimental animals was conducted. Results indicate that catecholamine fluorescence in the brain reduces and yellowish indoleamine fluorescence manifests after treatment with 5-hydroxytryptamine (5-HTP) alone and Ro4-4602 plus 5-HTP, suggesting that catecholamine is likely to be replaced by indoleamine. Ro4-4602 did not cause any change in central catecholamine neurons directly except in median eminence where the inhibitor caused a decrease in dopamine fluorescence. These findings suggest that the inhibitor may act in the hypothalamus in the same manner as in the peripheries. L-dopa alone and L-dopa plus R04-4602 enhance dopamine fluorescence in the substantia nigra and the median eminence, with an increase in the extraneuronal fluorescence seen especially in the latter. This indicates the release of amines from cell body into extraneuronal spaces. 12 references. (Author abstract modified)

229318 Kebabian, John W.; Bloom, Floyd E.; Steiner, Alton L.; Greengard, Paul. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Neurotransmitters increase cyclic nucleotides in postganglionic neurons: immunocytochemical demonstration.** Science. 190(4210):157-159, 1975.

Studies were undertaken in vertebrate sympathetic ganglia to determine intracellular increases in content of cyclic nucleotides in response to neurotransmitters. Results indicate that dopamine increases adenosine 3',5'-monophosphate (cyclic AMP) but not guanosine 3',5'-monophosphate (cyclic GMP) in slices of bovine sympathetic ganglion; this increase is localized

to the postganglionic neurons. Conversely, acetylcholine increases cyclic GMP but not cyclic AMP in the ganglion; this increase occurs within postganglionic neurons. Thus, different neurotransmitters can selectively alter cyclic nucleotide levels within the same neuronal population. 11 references. (Author abstract modified)

229431 Bunney, B. S.; Aghajanian, G. K. Yale University School of Medicine, New Haven, CT **Evidence for drug actions on both pre- and postsynaptic catecholamine receptors in the CNS.** Psychopharmacology Bulletin. 11(4):8-10, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 research reporting evidence for drug actions on both presynaptic and postsynaptic catecholamine receptors (auto receptors) in the central nervous system was reviewed, including biochemical findings, electrophysiological experimentation, and behavioral observations. Emphasis on the actions of a variety of antipsychotic drugs and their ability to block presynaptic and postsynaptic dopamine receptors. Such drugs include the various antipsychotic agents and amphetamine. Findings suggest the need to assess the effect and relative potency of drugs on both presynaptic and postsynaptic catecholamine receptors in order to fully understand the basis for their actions. 19 references. (Journal abstract modified)

229434 Creese, Ian; Iversen, Susan D. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD **Behavioural sequelae of dopaminergic degeneration: postsynaptic supersensitivity?** Psychopharmacology Bulletin. 11(4):12-13, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 the behavioral effects of drugs that are known to influence catecholamine function in rats subsequent to the bilateral lesion of the nigrostriatal dopamine system with 6-hydroxydopamine (6-OHDA) were discussed. The aim of the research was to determine the behavioral sequelae of dopaminergic degeneration and whether or not its results in postsynaptic supersensitivity. It was noted that results of numerous experiments with lesioned rats suggest this, but it is recommended that they be viewed with caution, since behavioral supersensitivity does not necessarily imply changes in the number or sensitivity of the receptor sites. Observations are required at the neuronal level or at the receptor site before definite conclusions can be reached. The most parsimonious explanation to date is that both presynaptic and postsynaptic mechanisms are responsible for the observed changes in reactivity to dopamine (DA) agonists which are seen following the interruption of the central DA pathways. 9 references. (Journal abstract modified)

229435 Iversen, L. L.; Horn, A. S.; Miller, R. J. MRC Neurochemical Pharmacology Unit, Medical School University of Cambridge, Cambridge, England **Structure activity relationships for agonist and antagonist drugs at pre- and postsynaptic receptor sites in rat brain.** Psychopharmacology Bulletin. 11(4):14, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 preliminary experimental results of research into the structure activity relationships for agonist and antagonist drugs at presynaptic and postsynaptic receptor sites in the rat brain were reported, stressing that dopamine (DA) stimulates cyclic AMP formation in homogenates of rat caudate/putamen by means of a specific DA sensitive adenylate cyclase. This system was examined as a model for studies of drug interactions at central nervous system DA receptors. Among DA analogues tested as potential agonists in this system, only apomorphine, 2-amino-6,7-dihydroxy, 1-2,3,4-tetrahydronaphalene, 1-(3,4-dihydroxyphenyl)-piperazine and epinine were as effective as DA in stimulating cyclic AMP formation. Neuroleptic drugs of various chemical classes proved to be potent inhibitors of the DA stimulated adenylate cyclase. Experiments with cholera toxin suggest that it is a valuable tool for investigating the cyclic AMP mediated mechanism in the CNS, and support the hypothesis that the postsynaptic actions of DA in the brain may be mediated by stimulation of adenylate cyclase activity. 3 references. (Journal abstract modified)

229436 Cuatrecasas, Pedro. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD **Criteria for and pitfalls in the identification of receptors.** Psychopharmacology Bulletin. 11(4):15, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 problems in the study of hormone receptors were discussed. The need for a solution was indicated, in order to continue the progress already made in identifying and analyzing cell membrane receptors for a variety of peptide, as well as nonpeptide, hormones and drugs. It was noted that many of the difficulties relate to the problem of nonspecific binding, while others concern identifying the precise kinetic constants of binding when the receptor concentration in the assay medium is exceptionally high, as is usually the case in binding studies which use ligands (hormones) of insufficiently high specific activity. In addition, assessment of binding affinity based on competition or displacement curves with native or unlabeled hormones underestimates the true affinity constant. 3 references. (Journal abstract modified)

229462 Fuxe, K.; Agnati, L.; Bolme, P. Department of Histology, Karolinska Institutet, Stockholm, Sweden **The possible involvement of GABA mechanisms in the action of benzodiazepines on central catecholamine neurons.** Psychopharmacology Bulletin. 11(4):55-56, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, an investigation of the possible involvement of gamma-aminobutyric acid (GABA) in the action of benzodiazepines on central chatecholamine neurons in rats was reported, focusing on dopamine (DA) turnover changes after benzodiazepines were administered. Evidence was obtained that two of the benzodiazepines, diazepam and chlordiazepoxide, may reduce DA turnover by increasing GABA receptor activity in the central nervous system (CNS). Reduction of DA turnover by diazepam was found in the same dose range that causes anticonvulsive effects and release of punished behavior. It is therefore possible that this action can be of importance for its antianxiety action. The primary action, however, is probably to increase GABA transmission in the CNS. It is possible that reduction of cortical noradrenaline (NA) turnover by high doses of benzodiazepines also involves an activation of a GABA-ergic mechanism in the locus coeruleus, which may be responsible for their sedative action. The blockade of stress induced increase in NA turnover may also be relevant to relief of anxiety. 6 references. (Journal abstract modified)

229463 Suria, Amin; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Diazepam depolarization of presynaptic terminals in bullfrog sympathetic ganglia: mediation through GABA?** Psychopharmacology Bulletin. 11(4):56-57, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, an investigation of diazepam depolarization of presynaptic terminals in bullfrog sympathetic ganglia was reported, which was designed to determine if the inhibition of posttetanic potentiation (PTP) by diazepam and dibutyryl cyclic guanosine 3',5'-monophosphate (diB cGMP) is mediated by the release of gamma-aminobutyric acid (GABA), which in turn may reduce the amount of transmitter released by depolarizing the preganglionic nerve terminals. It was found that the depolarization of nerve terminals elicited by diazepam may depend on the release of GABA located in the glial cells in this ganglion. The depolarization of nerve terminals elicited by GABA released by diazepam from the glial cells storage sites may decrease the amount of transmitter released from the preganglionic nerves by incoming stimuli. This inhibition may be particularly effective after the conditioning train and may explain the inhibition of PTP elicited by diazepam and diB cGMP. 12 references. (Journal abstract modified)

229464 Hess, S. M.; Chasin, M.; Free, C. A.; Harris, D. N. Squibb Institute for Medical Research, Princeton, NJ 08540 **Modulators of cyclic-AMP systems.** Psychopharmacology Bulletin. 11(4):57-58, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, a study of modulators of cyclic-3',5'-adenosine monophosphate (cyclic-AMP) systems in 159 drugs collected from 49 therapeutic classes in assays in vitro that reflect involvement with cyclic-AMP was reported. Included were tests using cell free and whole cell preparations of cyclic nucleotide phosphodiesterase (PDE) and adenylate cyclase. Although an unusually large number of drugs in the central nervous system and anti-infective classes were active in one or more of the tests, the mechanism of action of none of the classes could be definitely attributed to perturbation of cyclic-AMP. Surprisingly, PDE inhibition was a relatively common attribute of many of the classes. PDE inhibitors occurred seven times more often among the drugs than among compounds chosen at random that had no pharmacological activity. Specific data are included on the action of the pyrazolopyridines and benzodiazepines. (Journal abstract modified)

229465 Haefely, W.; Kulcsar, A.; Mohler, H. Department of Experimental Medicine, F. Hoffman-La Roche, Ltd., Basel, Switzerland **Possible involvement of GABA in the central actions of benzodiazepines.** Psychopharmacology Bulletin. 11(4):58-59, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, a study of the possible involvement of gamma-aminobutyric acid (GABA) in the central actions of benzodiazepines was presented which demonstrates that at least some effects of benzodiazepines are mediated through an interaction with GABA-ergic mechanisms. It is postulated from these data that benzodiazepines facilitate GABA-ergic transmission, thereby enhancing presynaptic and postsynaptic inhibition wherever it is mediated by GABA. While the anticonvulsant and muscle relaxant actions of benzodiazepines are well explained by this mode of action, the possible involvement of GABA in the sedative and anxiolytic actions of the drugs requires further study. (Journal abstract modified)

229466 Costa, E.; Guidotti, A.; Mao, C. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Involvement of GABA in the action of benzodiazepine -- studies on rat cerebellum.** Psychopharmacology Bulletin. 11(4):59-60, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, a study of the involvement of gamma-aminobutyric acid (GABA) in the action of benzodiazepine in rat cerebellum was reported. It was hypothesized that diazepam may act through a facilitation of the effects of endogenous GABA. Two indirect lines of evidence suggest that the pool of cyclic 3',5'-guanosine monophosphate (cGMP), which is decreased by an increase of cerebellar GABA content and by diazepam, resides in the Purkinje cells. Findings open new avenues for understanding of the action of benzodiazepines. New questions arise with regard to the dynamics that control the steady state of the transmitter in GABA-ergic neurons. Further, a possible role for the GABA storage in glial cells should be considered. Finally, the role of GABA neurons in anxiety and neurosis, for which diazepam appears to be the remedy of choice, should be studied. 8 references. (Journal abstract modified)

229474 Altura, Burton M. State University of New York, Brooklyn, NY **Interactions of alcohol, barbiturates, and narcotics with blood vessels.** Psychopharmacology Bulletin. 11(4):68, 1975.

The effects of ethyl alcohol, barbiturates, and narcotics and their antagonists on peripheral circulation are being investigated to contribute to development of pharmacologic regimens to treat the circulatory manifestations and depression brought about by intoxication with these drugs. Ss include rats, dogs, and rabbits; some in vitro studies may use human vascular material. In vivo microscopy is used to determine the precise mechanism of action and sites of the target compounds in circulatory vessels. In vitro studies with isolated vascular smooth muscle focus on the question whether acute administration has direct musculotropic effects. The effect of the drugs on blood vessels via indirect action (potentiating or inhibiting actions of circulating vasoactive agents) is also being studied. Experimentation is presently in the data collection stage. (Journal abstract modified)

229476 Bridgers, William F. University of Alabama, Birmingham, AL 35486 **Folic acid and behavior.** Psychopharmacology Bulletin. 11(4):69, 1975.

The effects of folic acid on brain chemistry and neurological functions are being investigated in mice. A method for synthesizing and purifying microscopic quantitites of tetrahydrofolate, N5, N10-methylene-tetrahydrofolate, and N5-methyl-tetrahydrofolate was developed. Injection of these derivatives along with 214C-folic acid and N5-14C-methyltetrahydrofolate indicated that brain uptake from the general circulation of these folates is extremely slow, while the clearance rates of intracerebrally injected folates are dependent upon whether or not the folate is in the tetrahydro form. Studies of the two major pathways responsible for endogenous production of one carbon folates indicate that the transhydroxymethylase enzyme was in brain mitochondria and in cytoplasm obtained by osmotic lysis of isolated synaptosomes. No formiminotransferase activity could be detected in mouse brain homogenates, suggesting that serine is the sole source of one carbon units in the brain. Methylenetetrahydrofolate dehydrogenase was present in the brain entirely as a soluble enzyme. Continued research may lead to better understanding of the methionine effect in schizophrenia. (Journal abstract modified)

229478 Cho, Arthur K. University of California, Los Angeles, CA 90024 **Chemistry and pharmacology of biogenic amine uptake.** Psychopharmacology Bulletin. 11(4):70, 1975.

Specific inhibitors of the uptake of norepinephrine, dopamine, and 5-hydroxytryptamine in the central nervous system are being synthesized. The compounds are based on amphetamine, and the aim is to increase understanding of the mode of action of psychoactive agents and develop means to study one of the essential steps of biogenic amine function at the molecular level. The basic amphetamine structure is modified by increasing lipophilicity and bulk to enhance specificity. In addition, reactive functional groups are introduced to prepare irreversible inhibitors which are to be used as active site labeling devices to quantitate and characterize the uptake. The biogenic amine carrier system is examined in vitro with rats using purified rat brain homogenates and nerve ending particles or synaptosomes and in vivo with conventional pharmacological procedures. (Journal abstract modified)

229480 Flynn, Edward J. College of Medicine and Dentistry of New Jersey, Newark, NJ **Immunologic investigation of barbiturate pharmacology.** Psychopharmacology Bulletin. 11(4):71, 1975.

Antibodies have been formed which have a specificity for interaction with barbiturate derivatives in mice and rabbits, and experiments are being conducted to increase the basic understanding of barbiturate metabolism and lead to an antidote for barbiturate toxicity. In one experiment, mice were actively immunized against barbiturates and tested for pharmacologic responsiveness to barbiturate administration. Similar tests are made with mice that have been passively immunized. A group of actively immunized rabbits serves as the source of barbiturate antibodies used to passively immunize the mice prior to pharmacological testing with barbiturates. In experiment two, the sensitivity of a radioimmunoassay method to measure barbiturates and their metabolic products is being explored, focusing on the capacity of extrahepatic tissues to metabolize drugs. Particular attention is directed to the brain, which is the target organ for the primary pharmacologic response. (Journal abstract modified)

229481 Forrest, Irene S. University of San Francisco, San Francisco, CA 94117 **Chlorpromazine excretion: isotope versus chemical assay.** Psychopharmacology Bulletin. 11(4):71-72, 1975.

Methodology for the quantitative determination of chlorpromazine (CPZ) and its metabolic products in the excreta is being developed in basic experiments with monkeys. Results are further tested in patients receiving CPZ therapy. Urine specimens of chronically dosed monkeys were subjected to sequential extraction of groups of CPZ metabolites following a 14C-CPZ test dose. Solvent extractions of the unconjugated metabolites showed satisfactory coincidence between radioquantitation and the sum total of nonphenolic and phenolic CPZ metabolites. Other studies indicate that the aqueous residue left after solvent extraction of the unconjugated CPZ metabolites contains the largest fraction of urinary CPZ in primates, and that it is the major source of the discrepancy between older techniques of radioquantitation and chemical assay. Further experimentation was performed on these findings and comparable results have been achieved in analyzing urine specimens of patients on chronic CPZ therapy. (Journal abstract modified)

229482 Friedel, Robert O. University of Washington, Seattle, WA 98105 **Biogenic amine effects on CNS phospholipid metabolism.** Psychopharmacology Bulletin. 11(4):72, 1975.

The effects of biogenic amines, hormones, and psychotropic drugs on the metabolism of receptor cells in the central nervous system (CNS) are under investigation in rats. Specifically, findings that adrenergic and cholinergic compounds have different initial effects on the metabolism of CNS phospholipids, and that the specificity of these effects is time dependent are being extended. In vivo studies of the effects of the drugs on incorporation of isotopically labeled phosphate into the major phosphorus acceptors, including phospholipids, phosphatidylinositol, and nucleotides, are being performed, along with examination of the subcellular localization of newly formed phospholipids synthesized in response to labeled phosphate and monoamines. In vitro studies are determining if the stimulation by acetylcholine or carbamylcholine of phosphatidylinositol and phosphatidic incorporation reflects enhanced synthesis or decreased catabolism. (Journal abstract modified)

229483 Fuxe, Kjell. Karolinska Institutet, Stockholm, Sweden **Neuroleptics and antidepressants on central monoamine neurons.** Psychopharmacology Bulletin. 11(4):72, 1975.

The mechanism of action of neuroleptics and antidepressants on the various central dopamine, norepinephrine, epinephrine, and serotonin pathways is under investigation in rats. Biochemical and functional studies of monoamine systems are combined with semiquantitative and quantitative amine fluorescence histochemistry and immunohistochemistry of catecholamine synthesizing enzymes. This approach facilitates regional analysis of monoamine cell bodies and terminals. Included are examination of the turnover of brain catecholamines following administration of alpha-methyl-paratyrosine or 3H-tyrosine, correlations between dopamine turnover and turning behavior or hypothermia, development of refined immunohistochemical methods for studying brain monoamine isozymes, and determination of the effects of thyrotropin releasing factor (TRF) on brain monoamine metabolism. (Journal abstract modified)

229486 Holmstedt, Bo R. Karolinska Institutet, Stockholm, Sweden **Analysis of drugs and psychoactive phenolic amines.** Psychopharmacology Bulletin. 11(4):74, 1975.

Psychoactive amines in biological fluids are being examined in normal adults and hospitalized patients, as well as in rabbits, mice and other animals, using a twofold process of isolation and pharmacologic evaluation. New methods have been developed which use both gas chromatography and mass spectrometry to study new compounds. Standard methods for identifying phenolic amines are also used, and the pharmacological investigations are conducted according to standard procedures. Over the course of study, new techniques have been developed for qualitative and quantitative analyses of nanogram to picogram quantities of compounds. Further, in a system developed for multiple ion detection, control of the gas chromatograph/mass spectrometer and signal processing components was confined to the computer, providing continual feedback and immediate hard copy display of calculated results. In another study, plasma concentrations of methaqualone were followed for several days after single oral doses in healthy Ss. Finally, application of mass fragmentographic techniques allowed accurate identification of nortriptyline and several of its metabolites in biological fluids from patients treated with therapeutic doses. (Journal abstract modified)

229489 Maas, James W. Yale University School of Medicine, New Haven, CT 06520 **Monoamines and mental illness.** Psychopharmacology Bulletin. 11(4):75, 1975.

The role played by specific brain amine systems in modulating, regulating, and controlling behavior in primates is being explored, focusing primarily on the anatomical identification of the various brain systems to gain knowledge of the neurobiological processes which underline normal and psychopathological behavioral patterns. Systems under study include the nigrostriatal dopamine system, the mesolimbic dopamine system, and the dorsal and ventral bundle norepinephrine systems in monkeys. These are stimulated electrically, emulating electrical stimulation by pharmacological means (amphetamine), and blocking influence of stimulation by specific interference with neurotransmitters using alpha-methyl-p-tyrosine, chlorpromazine, or pimozide. Histochemical and neurophysiological procedures are used to identify anatomical regions of the target systems. Reinforcement properties of brain stimulation, effects of negative reinforcement, and conditioned avoidance and suppression are measured via observing and codifying rating scales. (Journal abstract modified)

229490 Mycek, Mary J. College of Medicine and Dentistry, New Jersey Medical School, Newark, NJ **Brain-liver interrelationship in barbiturate tolerance.** Psychopharmacology Bulletin. 11(4):75-76, 1975.

The relative contributions of brain adaptation and hepatic metabolism in the production of tolerance to barbiturates are being examined in rats. Phenobarbital or barbital are administered intraventricularly by stereotaxically implanted cannulae. The hypnotic effect of the drugs is assessed by duration of loss of righting reflex. Following behavioral observation, the brain and liver are removed, and the hepatic microsomes are assayed for the enzymes, p-nitroanisole demethylase and hexobarbital oxidase. Results to date suggest that tolerance to phenobarbital can be produced by chronic central injection of the barbiturate; that it is a reversible phenomenon; that it can occur independent of the level of hepatic oxidative activity; and that it can be modified by central cholinergic and possibly adrenergic mechanisms. (Journal abstract modified)

229491 Reis, Donald J. Cornell University Medical College, New York, NY **The mechanism of action of amphetamine in brain.** Psychopharmacology Bulletin. 11(4):76, 1975.

The mode of action of amphetamines is being studied in rats, cows, and normal human Ss, focusing on the way in which this drug and its major metabolites modulate the activity and turnover of catecholamine synthesizing enzymes, including tyrosine hydroxylase, pteridine reductase, DOPA decarboxylase, and dopamine-beta-hydroxylase. The enzymes are purified and certain key properties are characterized. Specific antibodies are produced to each enzyme from the three species of Ss. The amount of enzyme regionally in the brain is measured by immunoprecipitation and radioimmunoassay methods; location is determined immunohistochemically. The action of amphetamine, p-hydroxyamphetamine, and p-hydroxynorephedrine on the kinetics of the purified enzyme materials is then examined in vitro. Finally, the action of acute and chronic administration of amphetamine and metabolites on the amounts of enzyme and rates of the synthesis and degradation in the brain is determined. (Journal abstract modified)

229494 Smith, Steven J. Pennsylvania State University, University Park, PA 16802 **Effects of psychotropic drugs on brain nuclear RNA.** Psychopharmacology Bulletin. 11(4):77-78, 1975.

Ties between nuclear RNA (ribonucleic acid) metabolism in specific brain subregions and the behavioral effects of various psychotropic agents are being investigated in male rats. Alterations of nuclear RNA metabolism are first examined during states of inhibition of ribosomal RNA synthesis and processing and during acute and chronic treatment with morphine, phenobarbital, amphetamine, lysergic acid diethylamide, delta9-tetrahydrocannabinol, and chlorpromazine. Alterations in nuclear RNA metabolism related to growth are then investigated. (Journal abstract modified)

229497 Sulser, Fridolin. Vanderbilt University, School of Medicine, Nashville, TN 37232 **Psychopharmacology research center.** Psychopharmacology Bulletin. 11(4):79, 1975.

The mechanism of action of psychotropic drugs in animals and men is being studied to develop a better understanding of the use of drug therapy in treating mental illness and to devise a more effective and safer chemotherapy of mental disorder. Rats, mice, and psychiatric patients are used as Ss, and the approach is broad and interdisciplinary. The following aspects of the pharmacology of psychotropic drugs are emphasized: the metabolic, neurochemical, and neurophysiological aspects of drug action; regulatory and adaptive mechanisms at presynaptic and postsynaptic sites of aminergic systems and their modification by drugs; interrelationships between various neuronal transmitter systems and their pharmacological modification; and the therapeutic characteristics of new agents. (Journal abstract modified)

229498 Tanner, N. Steven. North Dakota State University, Fargo, ND 58102 **Study of serotonin and ACTH brain levels and behavior.** Psychopharmacology Bulletin. 11(4):79, 1975.

The impact of changes in brain levels of serotonin (5-HT) and adrenocorticotrophin hormone (ACTH) on extinction of a conditioned avoidance response is being examined in rats to determine the mechanism by which they influence a specific form of behavior and their possible relationship to each other in the brain. Normal, hypophysectomized, and adrenalectomized Ss are conditioned in a shuttlebox in which an auditory stimulus precedes delivery of electric shock. Shock is not delivered if Ss shuttle in response to the stimulus. When Ss have learned to avoid shock, a 10 day extinction period begins. Brain tissues are analyzed during extinction for levels of 5-HT and norepinephrine, and blood samples are analyzed for corticosterone levels. Preliminary experiments in normal rats indicated that 5-hydroxytryptophan elevated brain 5-HT levels and increased resistance to extinction. p-Chlorophenylalanine decreased brain levels of 5-HT, decreased blood levels of corticosterone, and facilitated extinction. (Journal abstract modified)

230450 Wepierre, J.; Cohen, Y; Rapin, J. UER de Chimie Therapeutique, Centre d'Etudes Pharmaceutiques, 92290 Chatenay-Malabry, France /**Accumulation of labeled ephedrine, norephedrine, amphetamine and tyramine in pigmented and nonpigmented eyes of black and white rats.**/ Accumulation de l'ephedrine, de la norephedrine, de l'amphetamine et de la tyramine marquees au carbone 14 dans les yeux pigmentes et non pigmentes de deux races de rats. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(2):342-350, 1975.

The accumulation of four sympathomimetic amines was compared in pigmented and nonpigmented eyes of rats. Pigmented eyes of nonalbino rats were found to accumulate ephedrine, norephedrine and amphetamine. After 15 minutes, accumulation of ephedrine and amphetamine was larger than

of norephedrine. Accumulation occurred in melanin containing iris and choroid and in lacrymal glands which lack melanin. Accumulation of tyramine did not occur in eyes containing melanin. The nonpigmented eyes of albino rats did not accumulate any of the amines. It appeared that in pigmented eyes melanin was a site of loss of ephedrine, amphetamine and norephedrine; hence a smaller amount of drugs is available for interaction with adrenergic neurons and a smaller mydriatic effect occurs. Accumulation is possible when metabolism is low, as observed with alpha methylated amines. The four sympathomimetic amines used did not accumulate in the pigmented skin of black and white rats. 14 references. (Author abstract modified)

230451 Modak, A. T.; Stavinoha, W. B.; Weintraub, S. T. Dept. of Pharmacology, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Dichlorvos and the cholinergic system: effects on cholinesterase and acetylcholine and choline contents of rat tissues.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(2):293-301, 1975.

The inhibition of cholinesterase by 50mg/kg/5ml dichlorvos and subsequent recovery of enzyme activity were studied in various anatomically discrete brain regions of the rat and found to be uniform in all regions studied. This uniformity was not observed in liver, erythrocytes and plasma. Acetylcholine levels were elevated in brain areas from 48% to 171% at 15 minutes after treatment. However, a biphasic effect was seen on choline metabolism in the brain. The cortex was found to be more cholinergic than the striatum in terms of percent increase in acetylcholine and choline. 27 references. (Author abstract modified)

230453 Dyer, D. C.; Benington, F.; Morin, R. D. Dept. of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Antagonism of d-lysergic acid diethylamide and mescaline by 1-methyl-1,2,5,6-tetrahydropyridine-N,N-diethyl-carboxamide (THPC).** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(2):197-200, 1975.

In a study of the antagonistic effect of 1-methyl-1,2,5,6-tetrahydropyridine-N,N-diethyl-carboxamide (THPC), contractions of sheep umbilical vasculature induced by 5-hydroxytryptamine, mescaline and d-lysergic acid diethylamide (LSD) were antagonized by THPC, but THPC did not block contractile responses to angiotensin. Data are interpreted to support previous suggestions that certain chemical entities representing portions of the LSD molecule may be effectively studied as antagonists to the hallucinogens. Present data indicate that THPC is a weak 5-hydroxytryptamine receptor antagonist. 4 references. (Author abstract modified)

230454 Edney, S. M.; Downes, H. Dept. of Pharmacology, University of Colorado Medical Center, Denver, CO **Contractor effect of barbiturates on smooth muscle.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(2):180-196, 1975.

Four different convulsant barbiturates, thiopental, methohexital and pentobarbital were tested for in vitro contractor effects on rabbit jejunal segments, aortic strips and tracheal chains. The two convulsants that elicited lethal, tonic seizures in vivo contracted all three types of isolated preparation; however, two other convulsants that elicited intense, nonlethal, clonic seizures lacked contractor effect. Methohexital and pentobarbital also lacked contractor effect. In aortic strips, contractions induced by the two convulsants were not impaired by concentrations of phenoxybenzamine that blocked all contractor response to norepinephrine, acetylcholine or histamine. Thiopental also contracted aortic strips but the effect differed from that of the convulsants in that it was much less intense, was partially antagonized by pretreatment with phenoxybenzamine and was greatly potentiated by the presence of norepinephrine. Intense contractor effects, independent of adrenergic mechanisms, seem characteristic of a particular group of convulsant barbiturates; these are also similar with respect to structure, stimulant potency and seizure pattern. 34 references. (Author abstract modified)

230457 Spehlmann, Rainer. Veterans Administration Research Hospital, Chicago, IL **The effects of acetylcholine and dopamine on the caudate nucleus depleted of biogenic amines.** Brain (London). 98(Part 2):219-230, 1975.

A study was designed to test the hypothesis that the interruption of nigrostriatal connections leads to an imbalance between the actions of acetylcholine (ACh) and dopamine (DA), the major transmitter candidates in the caudate nucleus (CN). It has been proposed that the reduction of the striatal biogenic amines in Parkinson's disease leads to such an imbalance. Compared with neurons in intact cats, neurons in cats with long standing nigrostriatal lesions were more easily excited by ACh and less easily suppressed by DA. Results suggest that the depletion of the striatal amines by lesions decreases the neuronal suceptibility to DA and increases that to ACh, possibly changing the sensitivity or the number of the neuronal receptors of these agents. 50 references. (Author abstract modified)

230475 Wada, Juhn A.; Osawa, Takeshi; Corcoran, Michael E. Division of Neurological Sciences, Faculty of Medicine, University of British Columbia, Vancouver, B.C. V6T 1W5, Canada **Effects of tetrahydrocannabinols on kindled amygdaloid seizures and photogenic seizures in Senegalese baboons, Papio papio.** Epilepsia. 16(3):439-448, 1975.

In a study of the effects of cannabis derivatives on seizures, i.p. injections of delta-8-tetrahydrocannabinol (delta-8-THC) and delta-9-THC failed to affect myoclonic response to photic stimulation in Senegalese baboons (Papio papio). Both isomers of THC exerted dose related antiepileptic effects upon established kindled convulsions provoked by electrical stimulation of amygdala in the same species. Delta-9-THC was more potent than delta-8-THC in terms of both antiepileptic effects and general toxicity. The antiepileptic effects of the THC isomers are attributed to the suppression of propagation of the induced afterdischarge to distant cerebral structures, although high doses also seemed to suppress afterdischarge at the site of stimulation. 19 references. (Author abstract modified)

230478 Wada, Juhn A.; Wake, Akira; Sato, Mitsumoto; Corcoran, Michael E. Division of Neurological Sciences, University of British Columbia, 2075 Wesbrook Place, Vancouver, British Columbia V6T 1W5, Canada **Antiepileptic and prophylactic effects of tetrahydrocannabinols in amygdaloid kindled cats.** Epilepsia. 16(3):503-510, 1975.

The acute administration of delta-8-tetrahydrocannabinol (delta-8-THC) or delta-9-THC failed to affect partially developed or fully developed kindled amygdaloid seizures in cats. However, delta-9-THC was effective in suppressing focal afterdischarge in the stimulated amygdala when administered very early in kindling, before the development of any clinical manifestations. This finding suggested that chronic administration of delta-9-THC during kindling might block the process of seizure development. This was supported by the observation that three of four cats failed to kindle when treated with the

drug. The cat that failed to be protected by delta-9-THC was also insensitive to the general electroclinical effects of moderately high doses of delta-9-THC. The prophylactic activity of delta-9-THC is in contrasted to the ineffectiveness of diphenylhydantoin. 18 references. (Author abstract modified)

230600 Kebabian, John W.; Clement-Cormier, Yvonne C.; Petzold, Gary L.; Greengard, Paul. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Chemistry of dopamine receptors.** Advances in Neurology. 9:1-11, 1975.

Homogenates of the rat caudate nucleus were examined for evidence of dopamine sensitive adenylate cyclase activity. It was found that adenylate cyclase activity in caudate nucleus homogenates is stimulated by low concentrations of dopamine. Norepinephrine also stimulated adenylate cyclase activity, but at considerably higher concentrations. Similarities of the dopamine receptor found in homogenates of the rat caudate nucleus to the indirectly characterized dopamine receptor are discussed. Calculated inhibition constants of several phenothiazine derivatives and related compounds for dopamine sensitive adenylate cyclase of rat caudate nucleus and olfactory tubercle are also compared. It is concluded that the dopamine receptor in the mammalian central nervous system, as in the peripheral autonomic ganglion, is the dopamine binding portion of a dopamine sensitive adenylate cyclase. It is proposed that hypoactivity of this enzyme system in the caudate nucleus is an important factor in the development of parkinsonism like symptoms produced by antipsychotic agents.

230817 Levitt, M.; Mendlewicz, J.; Fleiss, J. L.; Fieve, R. R. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Norepinephrine metabolism in mouse heart after lithium and rubidium treatment.** Neuropsychobiology (Basel). 1(3):188-195, 1975.

The effects of treatment with lithium (Li), rubidium (Rb) and sodium (Na) for 7 days on norepinephrine (NE) turnover in mouse heart were examined. The effects of several drugs which modify the uptake and storage of NE were also studied in similarly pretreated mice. A method based on the combustion of tissue tritium to tritiated water was used to assay tritiated l-norepinephrine concentrations in individual hearts. The rate of decline of tissue tritium concentrations in groups of pretreated mice maintained at ambient temperature or in the cold was determined. The results indicate that, compared to Na, Li and Rb did not modify the tritium turnover rate in mouse heart. Pretreatment with Li or Rb did not modify the uptake of tritiated NE in the heart. The effects of desipramine, cocaine, bretylium and chlorpromazine on NE uptake were not altered by the alkali ions. Pretreatment did not modify NE release by tyramine, metaraminol and guanethidine. These studies suggest that Li and Rb do not modify NE uptake, release and storage in mouse heart. 25 references. (Author abstract)

230819 van Spanning, H. W.; van Zwieten, P. A. Department of Biopharmacy, University of Amsterdam, Amsterdam, The Netherlands **The interaction between alpha-methyl-dopa and tricyclic antidepressants.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(1):65-67, 1975.

The central hypotensive action of alpha-methyl-DOPA which was antagonized by tricyclic antidepressants like desipramine and imipramine was explored. This antagonism has been demonstrated in chloralose anesthetized cats. The drugs to be tested were infused into the left vertebral artery. It is suggested that the antagonism takes place in the pons medulla region of the central nervous system and that the alpha-adrenolytic properties of the tricyclic antidepressants bring about the blockade of central alpha-adrenergic receptors that are stimulated by alpha-methyl-noradrenaline, the biotransformation product of alpha-methyl-DOPA. 12 references. (Author abstract)

230826 Meltzer, Herbert Y. Department of Psychiatry, University of Chicago School of Medicine, Chicago, IL **Plasma creatine phosphokinase levels in rats following lysergic acid diethylamide.** Psychopharmacologia (Berlin). 44(1):91-93, 1975.

Plasma creatine phosphokinase (CRK) levels were measured in rats following lysergic acid diethy amide (LSD). LSD injected intraperitoneally or intramuscularly did not increase rat plasma CPK activity. LSD did not produce an increase in serum CPK activity in rats kept in a 2 degrees C environment for 2 hours. LSD also did not potentiate, in rats, the increase in plasma CPK activity produced by restraint at 2 degrees C or 24 degrees C. It is likely that the increases in serum CPK activity previously reported to occur in people who became psychotic following LSD ingestion are a consequence of the psychotic state itself rather than a direct effect of LSD. 23 references. (Author abstract)

230834 King, Lucy J.; Carl, Juanita L.; Lao, Lauro. Department of Psychiatry, Medical College of Virgina, Richmond, VA 23298 **Cocaine and amphetamine modification of cerebral energy metabolism in vivo.** Psychopharmacologia (Berlin). 44(1):43-45, 1975.

Alterations produced by cocaine and amphetamine on cerebral cortical energy metabolism during electrical stimulation were examined in mice in vivo. At the time of maximal behavioral stimulation after injection of amphetamine in mice, elevation of cerebral cortical levels of malate in the citric acid cycle and of the amino acid, alanine, was observed, suggesting that this drug has widespread effects on energy metabolism. Cocaine in contrast, produced elevation of brain glucose but not of citric acid cycle substrates or amino acids at the time of maximal hyperactivity. These observations are discussed in terms of the mechanisms of action of these two central nervous system stimulants. 10 references. (Author abstract)

230835 Houser, Vincent P.; Cash, Randall J.; Van Hart, Dale A. Route 94, Chester, NY 10918 **The effects of metiamide on the "activity-stress" ulcer in rats.** Psychopharmacologia (Berlin). 44(1):37-41, 1975.

The effects of metiamide on the activity/stress ulcer were examined in rats. The animals were equally divided into four groups that received either saline, 12.5mg/kg 25.0mg/kg or 50.0mg/kg of metiamide three times a day. All animals died within 11 days and all demonstrated significant gastric lesions in the glandular fundus of the stomach. The 50.0mg/kg dosage group, however, demonstrated significantly fewer ulcers than the saline animals and the lesions that did occur were significantly smaller than those noted in the control animals. Several hypotheses were offered to explain these results which took into account metiamide's effects on gastric secretion and motor activity. It was suggested that secretion of acid may be an important contributing factor in the formation of gastric ulcers in animals subjected to the activity/stress procedure. 9 references. (Author abstract)

230840 Shih, Tsung-ming; Khachaturian, Zaven S.; Barry, Herbert, III; Reisler, Kurt L. Department of Psychiatry,

University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15261 **Differential effects of methylphenidate on reticular formation and thalamic neuronal activity.** Psychopharmacologia (Berlin). 44(1):11-15, 1975.

The neural structures affect by methylphenidate and the nature of this drug's effect on unit discharges recorded from both rats and cats were examined. Intravenous administration of methylphenidate markedly attenuated the unit discharge rate in the mesencephalic reticular formation of rats and cats. Concurrently this drug enhanced the neural activity in the primary sensory nuclei of the thalamus. The differential effects of methylphenidate on these two neural systems suggest a possible mechanism by which it may improve attentive processes in hyperkinesis. 29 references. (Author abstract)

230841 Breese, George R.; Cooper, Barrett; Hollister, Alan S. Department of Psychiatry, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Involvement of brain monoamines in the stimulant and paradoxical inhibitory effects of methylphenidate.** Psychopharmacologia (Berlin). 44(1):5-10, 1975.

The significance of central noradrenergic, dropaminergic and serotonergic neural systems for the locomotor stimulant effects of methylphenidate was investigated in the rat. Methylphenidate stimulate motor activity was antagonized by alpha-methyltyrosine and enhanced after treatment with U-14,624, a dopamine-beta-hydroxylase inhibitor, suggesting that release of newly synthesized dopamine is important to a locomotor stimulant action of methylphenidate. Evidence implicating brain serotonin in the actions of methylphenidate was obtained in rats pretreated with pargyline or p-chlorophenylalanine (PCPA). Administration of pargyline 1 hr prior to methylphenidate was found to reduce the locomotor activity induced by methylphenidate and this was antagonized by pretreatment with low doses of PCPA. Higher doses of PCPA caused a significant elevation of methylphenidate induced activity which could be reduced by 5-hydroxytryptophan. Destruction of serotonergic neurons with 5,7-dihydroxytryptamine also potentiated methylphenidate induced locomotion. The findings suggest that serotonergic fibers have an inhibitory function in brain. These results are discussed in relation to the possible mechanism by which methylphenidate may act in hyperkinesis. 24 references. (Author abstract modified)

230853 Peters, D. A. V.; Mazurkiewicz-Kwilecki, I. M. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario **Tyrosine hydroxylase activity in rat brain regions after chronic treatment with plus/minus-propranolol.** Journal of Pharmacy and Pharmacology (London). 27(9):671-676, 1975.

Tyrosine hydroxylase activity was examined in rat brain regions after chronic treatment with plus/minus-propranolol. Rats were injected twice daily with plus/minus propranolol for 14 days and killed 16 h after the final injection. Tyrosine hydroxylase activity was measured in both soluble and particle bound forms in various brain regions. The activity of the soluble enzyme was not significantly altered by propranolol treatment in any of the brain regions studied. The tyrosine hydroxylase activity in the particulate fraction was significantly increased in corpus striatum and unchanged in other brain regions. The propranolol concentrations in the various brain regions in this chronic study were far lower than necessary to produce a significant change in tyrosine hydroxylase activity in acute experiments. It was concluded that chronic propranolol treatment produces a persistent increase in bound tyrosine hydroxylase activity in rat corpus striatum. 26 references. (Author abstract)

230854 Javoy, France; Agid, Yves; Glowinski, Jacques. Groupe NB, INSERM U.114, College de France, 11, place Marcelin Berthelot, 75231 Paris Cedex 05 **Oxotremorine- and atropine-induced changes of dopamine metabolism in the rat striatum.** Journal of Pharmacy and Pharmacology (London). 27(9):677-681, 1975.

The effects of various doses of oxotremorine and of atropine on the metabolism of dopamine were examined in the striatum of the rat. Changes in striatal dopamine metabolism were estimated by following either the accumulation of (3H)dopamine 15 min after intravenous injection of (3H)tyrosine or the accumulation of dopa in animals pretreated with a dopa decarboxylase inhibitor (Ro4-4602). Oxotremorine and atropine did not affect dopamine metabolism. Oxotremorine did not modify dopamine concentrations but increased the accumulation of (3H)dopamine. The drug enhanced dopa formation in animals pretreated with Ro4-4602. Atropine increased the accumulation of (3H)dopamine but did not affect dopamine concentrations. The accumulation of dopa was not modified there was no difference from the saline value in animals pretreated with the dopa decarboxylase inhibitor. Thus at high doses oxotremorine stimulated dopamine metabolism and atropine reduced dopamine utilization. 23 references. (Author abstract)

230855 Jenner, P.; Chadwick, D.; Reynolds, E. H.; Marsden, C. D. University Department of Neurology, Institute of Psychiatru, De Crespigny Park, London SE5 **Altered 5-HT metabolism with clonazepam, diazepam and diphenylhydantoin.** Journal of Pharmacy and Pharmacology (London). 27(9):707-710, 1975.

The effects of clonazepam on mouse brain 5-hydroxytryptamine (5-HT) metabolism were examined and compared to the effects of diazepam and diphenylhydantoin (DPH). The typical increase in 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) observed after the acute administration of clonazepam was not evident following chronic treatment with high doses of the drug for 8 days. This dose dependent increase in 5-HT and 5-HIAA after clonazepam treatment occurred at much lower doses than for either diazepam or DPH administration. It is suggested that diazepam interferes with the metabolism of the parent amine and that clonazepam may increase the rate of synthesis of 5-HT and to a lesser extent its release. 22 references.

230856 Bracs, P.; Jackson, D. M.; Chesher, G. B. Department of Pharmacology, University of Sydney, N.S.W. 2006, Australia **The effect of delta9-tetrahydrocannabinol on brain amine concentration and turnover in whole rat brain and in various regions of the brain.** Journal of Pharmacy and Pharmacology (London). 27(9):713-715, 1975.

The effects of delta9-tetrahydrocannabinol (THC) on both endogenous levels and turnover of brain noradrenaline, dopamine and 5-hydroxytryptamine (5-HT) were examined in the rat brain. No significant changes were observed in either whole brain concentrations of dopamine, noradrenaline or 5-HT or in noradrenaline or 5-HT concentrations in the neostriatum, hypothalamus plus midbrain, thalamus, cerebellum, pons - medulla or in dopamine concentrations in neostriatum or hypothalamus plus midbrain thalamus on the administration of high doses of THC. The results suggest that comparatively high doses of THC are without effect on either endogenous concentrations of 5-HT, noradrenaline or dopamine, or dopamine and noradrenaline turnover. 27 references.

230859 Leeuwin, R. S.; Djojodibroto, R. D.; Groenewoud, E. Th. Pharmacological Laboratory, Polderweg 104, University of Amsterdam, Amsterdam, The Netherlands **The effects of three benzodiazepines and of meprobamate on the action of smooth muscle stimulants on the guinea-pig ileum.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(1):18-21, 1975.

The effects of three benzodiazepines and of meprobamate were examined on the action of smooth muscle on the guinea-pig ileum. The benzodiazepines chlorodiazepoxide, diazepam and flurazepam, and of meprobamate depress the response of the guinea-pig ileum to acetylcholine, histamine and 5-hydroxytryptamine. As compared to the benzodiazepines the action of meprobamate is very weak. Chlordiazepoxide has a weaker anticholinergic activity than diazepam and flurazepam. On the other hand chlordiazepoxide possesses a relatively strong antihistamine activity. The three benzodiazepines tested are about equally effective in reducing the contraction of the guinea-pig ileum caused by 5-hydroxytryptamine. The potency of diazepam and flurazepam in blocking the effect of the three smooth muscle stimulants appears to be rather similar. 9 references. (Author abstract)

230860 Bonfitto, M.; Della Bella, D.; Santini, V. Zambon, S.p.A. Research Laboratories, Bresso-Milan, Italy **Study of the action of some centrally acting drugs on the EEG and on a conditioned avoidance reflex in the rabbit.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(1):131-139, 1975.

The effect of perphenazine, diazepam, benactyzine, morphine and a new central analgesic, viminol were examined on both electroencephalogram and behavior in rabbits with chronically implanted electrodes trained to a conditioned escape reflex. The results obtained are discussed in terms of the mechanism and site of action of the different drugs. The experimental procedure adopted is recommended to obtain additional information on the properties of centrally acting drugs. 2 references. (Author abstract)

230862 Berry, Douglas G. Department of Anesthesiology, University of Minnesota Health Sciences Center, Minneapolis, MN 55455 **Effects of diazepam on the isolated chick embryo heart.** Proceedings of the Society for Experimental Biology and Medicine. 150(1):240-243, 1975.

The effects of diazepam were observed in the noninnervated 4-day-old embryonic heart as well as in the innervated 7-day-old embryonic heart of the chick. Diazepam decreased the rate and amplitude of contraction in isolated embryonic chick hearts in a dose dependent manner in both the noninnervated hearts obtained from 4-day-old embryos and the innervated hearts from 7-day-old embryos. Prior administration of atropine did not alter the depression induced by diazepam. Norepinephrine was able to stimulate the amplitude of contraction in the diazepam depressed heart while atropine was without effect. The vehicle used in the clinical injectable preparation of diazepam had no depressant effects. The mechanism of action of the diazepam induced depression on the isolated embryonic chick heart may be a direct depression of the myocardium. 26 references. (Author abstract modified)

230918 Sundaresan, P. R.; Rivera-Calimlim, L. Department of Pharmacology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Distribution of chlorpromazine in the gastrointestinal tract of the rat and its effect on absorptive function.** Journal of Pharmacology and Experimental Therapeutics. 194(3):593-602, 1975.

The distribution of carbon labeled chlorpromazine was studied in segments of the gastrointestinal tract of the rat after an oral dose of 20mg/kg. The maximum observed total radioactivity in the different segments occurred at different times after dosing. The percentage of total radioactivity present in each tissue as unchanged labeled chlorpromazine decreased with time in all the tissues. At all time points, this parameter also showed a consistent pattern, with declining percentages of unchanged chlorpromazine radioactivity in the stomach duodenum, jejunum and ileum respectively. The effect of chronic administration of labeled chlorpromazine on intestinal absorptive function was studied by the everted sac technique. Mucosal transport of labeled methionine was significantly inhibited, but no effect on transport labeled D-xylose was observed. 30 references. (Author abstract modified)

230919 Lee, Cheng-Yi Akera, Tai; Stolman, Sheldon; Brody, Theodore M. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Saturable binding of dihydromorphine and naloxone to rat brain tissue in vitro.** Journal of Pharmacology and Experimental Therapeutics. 194(3):583-592, 1975.

The binding in vitro of an opiate agonist, 3H-dihydromorphine, was studied using a particulate fraction obtained from rat brain homogenates and compared with that of an opiate antagonist, 3H-naloxone. The binding of 3H-dihydromorphine may be separated into two components: one a saturable component and the other nonsaturable. The saturable binding may be calculated from the differences in binding observed in the absence and presence of high concentrations of levorphanol. It appeared that the saturable binding sites from various brain regions had similar affinities for dihydromorphine except for the binding site from cerebral cortex which had a higher affinity. In contrast, saturable binding sites for naloxone in various brain regions had different affinities for naloxone. It appears that naloxone has at least two types of saturable binding sites, one of which is not available to dihydromorphine. It is concluded that naloxone binds to dihydromorphine binding site and to another site, which has a different affinity for naloxone and is not available to dihydromorphine. 19 references. (Author abstract modified)

231002 Blasberg, R. G.; Patlak, C.; Fenstermacher, J. D. National Cancer Institute, Bldg. 37, Room 5A17 Bethesda, MD 20014 **Intrathecal chemotherapy: brain tissue profiles after ventriculocisternal perfusion.** Journal of Pharmacology and Experimental Therapeutics. 195(1):73-83, 1975.

Ventriculocisternal perfusions with five isotopically labeled drugs were performed in the rhesus monkey and the resultant tissue diffusion concentration profiles in caudate nucleus were analyzed. The periventricular distribution space with respect to perfusate concentration was measured and expressed as microliters per 100mg wet weight: hydroxyurea = 56; methotrexate = 27; thiotepa = 28; 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) = 64 and cytosine arabinoside = 170. Capillary permeability expressed as an extracellular space/transcapillary exchange half time was estimated to be greater than 2 hours for both compounds. Cytosine arabinoside continued to be concentrated by periventricular caudata nucleus during the course of perfusion; perfusate clearance measurements suggest a low capillary permeability. The apparent parenchymal diffusion constant and the capillary permeability of a drug in brain are discussed and are considered useful parameters for predicting drug levels after intrathecal administration. 31 references. (Author abstract modified)

231003 Shoeman, Don W.; Azarnoff, Daniel L. Clinical Pharmacology-Toxicology Research Center, 3800 Cambridge, Kansas City, KS 66105 **Diphenylhydantoin potency and plasma protein binding.** Journal of Pharmacology and Experimental Therapeutics. 195(1):84-86, 1975.

Rats were given diphenylhydantoin (DPH) orally, and its potency in protecting against maximal electroshock seizures was determined. The effect of an intravenous dose of 100mg of phenylbutazone per kg 1 hour before testing on the potency and on the total and unbound plasma concentration of DPH was then measured. Phenylbutazone treatment incireased the potency of DPH in terms of dose and total drug concentration but did not affect the potency of unbound DPH. The anticonvulsant action of DPH depends upon the concentration of unbound drug in plasma and not upon total plasma concentration nor upon dose. 18 references. (Author abstract)

231004 Cook, Jay D.; Schanberg, Saul M. Building 10, NINDS, NIH, Bethesda, MD 20014 **Effect of methamphetamine on norepinephrine metabolism in various regions of brain.** Journal of Pharmacology and Experimental Therapeutics. 195(1):87-93, 1975.

The effects of methamphetamine on tritiated and endogenous norepinephrine metabolism was examined in various regions of brain. In acute experiments, 30 minutes or 5 hours after methamphetamine i.p.,3H-norepinephrine was injected into the cisterna magna. In rats treated acutely, methamphetamine caused a significant block in uptake of 3H-norepinephrine and a marked increase in the content of 3H-normetanephrine in all regions except the cortex. Five hours after methamphetamine administration, increased levels of 3H-norepinephrine occurred in the pons/medulla, whereas endogenous norepinephrine content tended to decrease in most regions. In rats treated chronically, enhanced accumulation of 3H-norepinephrine was also confined to the pons-medulla region, whereas endogenous levels of norepinephrine were high in the pons/medulla and low in the hypothalamus and cortex. These data suggest that chronic administration of methamphetamine, affects either catecholaminergic nerve cell bodies or nerve terminals in the pons/medulla differentially, as compared to other regions studied. 24 references. (Author abstract modified)

231006 Weaver, Lynne C.; Akera, Tai; Brody, Theodore M. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Opposing responses in sympathetic nerve activity induced by central injections of ouabain.** Journal of Pharmacology and Experimental Therapeutics. 195(1):114-125, 1975.

The central action of ouabain on sympathetic outflow was examined in baroreceptor and chemoreceptor denervated cats. Ouabain was injected into 128 vasoconstrictor or cardioaccelerator sites in the medulla or hypothalamus. Electrical stimulation of 24% of these sites evoked arrhythmias and stimulation consistently caused marked increases in heartrate, blood pressure and nerve activity, but ouabain had several effects, inducing either no change or increases or decreases in spontaneous activity of vasoconstrictor and cardioaccelerator nerves. In general, spontaneous and evoked activities were inhibited by ouabain more frequently than they were enhanced. The pattern of nervous responses to ouabain did not relate to the dose of drug or to the anatomical site of injection. Central microinjections of ouabain produced heterogenous patterns of effects on activity of peripheral sympathetic nerves, and these microinjections were not sufficient to evoke cardiac arryhthmias in cats with sectioned cranial nerves IX and X. 45 references. (Author abstract modified)

231007 Whitehouse, L. W.; Paul, C. J.; Coldwell, B. B.; Thomas, B. H. Drug Research Laboratories, Health Protection Branch, Health and Welfare Canada, Ottawa, Ontario, Canada K1A OL2 **Effect of ethanol on diazepam distribution in rat.** Research Communications in Chemical Pathology and Pharmacology. 12(2):221-242, 1975.

The effect of an acute oral dose of ethanol administered 30 min prior to oral administration of 14C-diazepam, on the fate of radioactivity in rats was examined. Ethanol pretreated rats possessed higher tissue levels at 60, 90 and 120 min than control animals. Blood, liver, kidney and plasma tissues showed 1.5fold differences, adipose tissue exhibited a 2.4to 3.6fold increase, with brain showing 3.9, 4.5and 5.4fold higher levels of 14C at 60, 90 and 120 min. respectively. Octanol extraction of plasma and ethyl acetate extraction of brain tissues indicated ethanol pretreated animals possessed a higher percentage of extractable radioactivity than controls. Thin layer chromatography of the extracts suggested that biotransformation of 14C-diazepam was inhibited by ethanol, causing brain levels of 14C-diazepam at 60 min to be 6.4fold higher than that observed in controls. 30 references. (Author abstract)

231008 Darvas, F.; Budai, Z.; Petocz, L.; Kosoczky, I. NIM IGUSZI, 1363 Budapest, P.O. Box 33, Budapest, Hungary **Substituted cycloalkanol ethers of psychostimulant activity: studies on quantitative structure-activity relationships.** Research Communications in Chemical Pathology and Pharmacology. 12(2):243-254, 1975.

Quantitative relationships between chemical structures and locomotor activities of 20 substituted cycloalcanol basic ethers were investigated in mice using Hansch and Free-Wilson methods. The Hansch type regression analysis performed on 10 compounds having different cycloalkyl rings revealed the highly significant role of the hydrophobic characteristics on the activity tested. On the basis of the results the compounds appear not to exert their activity through interaction with receptor raising strict sterical and electrical requirements. 11 references. (Author abstract modified)

231009 Buckingham, R. L.; Radulovacki, M. Dept. of Pharmacology, College of Medicine, University of Illinois, Chicago, IL 60680 **The selective effects of alpha-methyl aromatic amino acids on brain monoamine metabolites and behavior in cats.** Research Communications in Chemical Pathology and Pharmacology. 12(2):255-265, 1975.

The effects of alpha-methyl aromatic amino acids on brain monoamine metabolites and behavior were examined in cats. Alpha-methyldopa or alpha-methylmetatyrosine were administered orally to cats and the electroencephalogram (EEG) recorded for 9 hours. Through the first 6 hours after each administration, the concentration of cisternal cerebrospinal fluid (CSF)5-hydroxyindoleacetic acid (5-HIAA) selectively decreased from control (hour 0) while homovanillic acid (HVA) levels showed only small changes. On observation, the animals were quiet but awake. At 9 hours after alpha-methyldopa administration, the percentage decrease of 5-HIAA was significantly greater from the percentage decrease of HVA. The EEG record from 6-9 hours following either drug showed fewer intervals of EEG synchronizaiton in both duration and frequency. These results indicate that behavior and EEG can be related to changes in brain monoamine metabolism determined in CSF. After either drug administration, dopamine turnover (as indicated by HVA) was higher than that of serotonin (as indicated by 5-HIAA) which corresponded to EEG desynchronization and other behavioral indicators of wakefulness. 18 references. (Author abstract)

231010 Chiu, Pauline; Karler, Ralph; Craven, Catherine; Olsen, Donna M.; Turkanis, Stuart A. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **The influence of delta9-tetrahydrocannabinol, cannabinol and cannabidiol on tissue oxygen consumption.** Research Communications in Chemical Pathology and Pharmacology. 12(2):267-286, 1975.

The mechanisms of the hypothermia produced in mice by the naturally occurring cannabinoids, delta9-tetrahydrocannabinol, cannabinol, and cannabidiol, was investigated by evaluating the direct effect of these drugs on the oxygen consumption of tissue homogenates and isolated mitochondria. The tissues studied were brain, liver, skeletal muscle, and heart; the mitochondrial preparations were limited to brain and skeletal muscle. The in vitro studies included a description of the influence of various cannabinoid vehicles containing Tween 80, ethanol, Pluronic F68, and albumin on the oxygen consumption of tissue preparations. In spite of the different vehicle effects, delta9-tetrahydrocannabinol generally reduced oxygen consumption of all tissue preparations; however, the vehicles were capable of modifying the dose effect relationship. The findings demonstrate that the cannabinoids can directly decrease oxidative metabolism of tissue and isolated mitochondria and suggest that the depressant effect of the cannabinoids on metabolic rate may contribute to the mechanism of the hypothermia produced by the drugs. 9 references. (Author abstract modified)

231011 Stolman, Sheldon; Loh, Horace H. Department of Pharmacology, University of California, San Francisco, CA 94143 **Barbital-induced cross-tolerance to barbiturates by the intracisternal route of administration.** Research Communications in Chemical Pathology and Pharmacology. 12(2):309-316, 1975.

Barbital induced cross-tolerance to barbiturates by intracisternal route of administration is reported in rats. Male rats receiving 2.4mg of barbital sodium intracisternally every 3 hours for four injections exhibited a significant decrease in sleeping time over that of control animals when challenged with pentobarbital 17 hours after the last pretreatment. These tolerant animals did not show a significant increase in either (14C)-leucine incorporating activity or hepatic aminopyrine demethylase activity. This intracisternal induced cross-tolerance to pentobarbital is apparently not due to hepatic enzyme induction, but may be related to an altered sensitivity of the central nervous system to these agents. 11 references. (Author abstract modified)

231014 Rudolph, Stephen A.; Greengard, Paul. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Regulation of protein phosphorylation and membrane permeability by beta-adrenergic agents and cyclic adenosine 3′:5′-monophosphate in the avian erythrocyte.** Journal of Biological Chemistry. 249(17):5684-5687, 1974.

Membrane protein phosphorylation in turkey erythrocytes was used to provide an explanation for catecholamine induced changes in cation permeability of these cells. The beta-adrenergic agonist, l-isoproterenol, stimulated the incorporation of 32P into a single membrane bound protein of the intact turkey erythrocyte with approximately the same time course with which it increased membrane permeability to sodium. The beta-adrenergic blocking agent, propranolol, abolished this effect. Exogenous adenosine 3′:5′-monophosphate (cAMP) and N6-monobutyryl cAMP mimicked the effect of isoproterenol. The phophoprotein was estimated to have an apparent molecular weight of 240,000 and was coincident with the protein band characteristic of erythrocyte plasma membranes known as Band II. Increased phosphorylation of this protein was observed to correlate with increased cAMP levels and increased sodium uptake in response to various agents. 19 references. (Author abstract modified)

231039 Antonaccio, M. J.; Halley, Jeanne. Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **Inhibition of centrally-evoked pressor responses by diazepam: evidence for an exclusively supramedullary action.** Neuropharmacology (Amsterdam). 14(9):649-657, 1975.

The inhibitory effects of diazepam on diencephalic, tegmental and medullary pressor sites were examined in cats. There was little or no effect on either resting blood pressure or responses to bilateral carotid artery occlusion with diazepam. Responses, either pressor or depressor to medullary paramedian reticular formation stimulation, or pressor to dorsolateral medullary stimulation were not inhibited at any current strength by either dose of diazepam. Pressor and tachycardic responses to fastigial nucleus stimulation in the cerebellum, which acts through the paramedian reticular formation, were not inhibited by diazepam. It appears that diazepam acts to inhibit evoked sympathetic responses throughout supramedullary sympathetic centers rather than on hypothalamus exclusively, and that resting sympathetic tone and baroreceptor responses are mediated through functionally different central structures than evoked sympathetic responses from supramedullary centres. 35 references. (Author abstract modified)

231070 Nemtsov, A. V.; Rad'ko, K. A. Moskovskogo nauchno-issledovatel'skogo instituta psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow, U.S.S.R. **/The effect of trifluoperazine on the transmission of excitation in the rabbit brain during prolonged administration of the preparation./** Vliyaniye triftazina na peredachu vozbuzhdeniya v golovnom mozge krolika pri dlitel'nom vvedenii preparata. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 80(8):63-66, 1975.

The effect of trifluoperazine administration on the transmission of excitation in the brain was investigated in rabbits exposed to daily doses of 1mg/kg for 2 weeks. The reaction of the cortical neurons in response to electrical stimulation of their adjacent areas was also studied. The dispersions of poststimulus histograms were measured, and it was found that trifluoperazine reduced the value and duration of the responses of the cortical neurons after stimulation. It is concluded that prolonged tifluoperazine administration aggravated the signal conduction in the neuron reticula. 10 references. (Journal abstract modified)

231071 Avakyan, R. M.; Arushanyan, Ye. B. Kafedra farmakologii, meditsinskogo instituta, Chita, U.S.S.R. **/The effect of catecholaminergic substances on proconvulsive properties of the caudate nucleus./** Vliyaniye katekholaminergicheskikh sredstv na prokonvul'sivnyye svoystva khvostatogo yadra. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 80(8):66-69, 1975.

The effect of catecholaminergic substances on proconvulsive properties of the caudate nucleus was investigated in freely moving rats. Stimulants of catecholaminergic transmission reduced the proconvulsive properties of the caudate nucleus. In rats under the influence of these stimulants, a shortening of the cortical electroencephalographic response to a single stimulation of the nucleus was noted in response to subconvulsive doses of pentylenetetrazol; the extent of the spike/wave rhythm was reduced following repeated caudate stimuli. The

inhibitors of catecholaminergic transmission, on the other hand, intensified the proconvulsive effect of the caudate nucleus. 6 references. (Journal abstract modified)

231304 Mishra, Ram K.; Demirjian, C.; Katzman, R.; Makman, N. H. Department of Biochemistry, Albert Einstein College of Medicine, Bronx, NY 10461 **A dopamine-sensitive adenylate cyclase in anterior limbic cortex and mesolimbic region of primate brain.** Brain Research (Amsterdam). 96(2):395-399, 1975.

The presence and properties of adenylate cyclase activity in homogenates of primate anterior limbic cortex and subcortical limbic regions (nucleus accumbens and olfactory tubercle) dopamine and neuroleptic drugs. The adenylate cyclase from anterior limbic cortex was stimulated by dopamine. In contrast, isopropylnorepinephrine and norepinephrine required at least a 1000 fold greater concentration to obtain an equivalent effect to dopamine. The maximal effects produced by isopropylnorepinephrine and norepinephrine were much less than that produced by dopamine or other dopamine agonists. The stimulatory effect of dopamine and dopamine agonists was selectively inhibited by antipsychotic drugs such as fluphenazine and haloperidol but not by the beta-adrenergic blocking agent, propranolol, or by the alpha-adrenergic blocking agent, phentolamine. These experiments suggest that dopamine and other dopamine agonists interact specifically with the postsynaptic dopamine receptors and in turn stimulate adenylatecyclase associated with such receptors. 18 references.

231438 Rosloff, Barry Noel. Vanderbilt University **Studies on the mechanism of action of tricyclic antidepressant drugs, using iprindole as a tool. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-21606 HC$13.50 MF$5.00 260 p.

The effects of chronic iprindole treatment on rat brain norepinephrine (NE) were examined and compated to those of desmethylimipramine (DMI) to evaluate the mechanism of action of tricyclic antidepressant drugs. Results indicate that chronic DMI treatment enhances brain NE decline after NE synthesis inhibition, but that tnis treatment decreases the NE version index, suggesting a decreased turnover. Chronic iprindole treatment however, did not affect NE turnover with either method. The effects of acute administration of DMI or iprindole on brain NE turnover were also studied, and results show that DMI decreased the conversion index, but produced no effect using the snythesis inhibition method. Iprindole did not affect the index but enhanced NE decline after synthesis inhibition. The significance of these changes in turnover are discussed in relation to current concepts of noradrenergic neuronal physiology and the catecholamine hypothesis of affective disorders. Findings also suggest that chronic DMI decreased brain NE levels by 10% to 15%, but neither acute nor chronic DMI or iprindole affected brain dopamine turnover or levels. Finally, neither acute nor chronic DMI or iprindole significantly affected brain choline acetyltransferase activity measured in vitro. (Journal abstract modified)

231700 Hoebel, Bartley G.; Hernandez, Luis; Thompson, Roger D. Department of Psychology, Green Hall, Princeton University, Princeton, NJ 08540 **Phenylpropanolamine inhibits feeding, but not drinking, induced by hypothalamic stimulation.** Journal of Comparative & Physiological Psychology. 89(9):1046-1052, 1975.

Suppression of hypothalamically induced eating without suppression of drinking induced by the same electrode was studied in Sherman rats using phenylpropanolamine. Phenylpropanolamine was found to inhibit only feeding, an effect which occurred whether feeding and drinking were tested simultaneously or separately. Selective inhibition of lateral hypothalamic feeding also followed injection of this drug through lateral, but not medial, hypothalamic electrode cannulas. It is concluded that hypothalamically induced feeding is under some of the same pharmacological controls as spontaneous feeding, that this control is exerted, in part, in or near the lateral hypothalamus, and that the neural systems which induce feeding and drinking during hypothalamic stimulation can be pharmacologically separated. 26 references. (Author abstract)

231701 Hatton, Daniel C.; Woodruff, Michael L.; Meyer, Merle E. University of Florida, Gainesville, FL 32611 **Cholinergic modulation of tonic immobility in the rabbit (Oryctolagus cuniculus).** Journal of Comparative & Physiological Psychology. 89(9):1053-1060, 1975.

The effects of the anticholinergic agent scopolamine and the cholinergic agent physostigmine on tonic immobility in rabbits were determined. Recordings of the electroencephalographic (EEG) activity from cortex and hippocampus were also made before, during, and after each test session. Scopolamine significantly prolonged the response and produced large amplitude slow wave activity in the EEG of both cortex and hippocampus. Physostigmine significantly shortened the duration of immobility and increased rhythmic slow activity in the frequency range of 5.5Hz to 9.1Hz in the hippocampus while producing a desynchronized cortical rhythm. It is hypothesized that the cortex and hippocampus play a role in modulating tonic immobility duration by inhibiting the brainstem structures thought to control this response. 11 references. (Author abstract)

231719 Bigler, Erin D. Division of Neurobiology, Barrow Neurological Institute of St. Joseph's Hospital, Phoenix, AZ 85013 **Lateral geniculate multiple-unit activity related to Metrazol potentiated after-discharges.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 39(5):491-497, 1975.

Lateral geniculate nucleus (LGN) multiple unit activity (MUA) related to Metrazol potentiated afterdischarges was investigated in male Holtzman rats. Following parenteral administration of subconvulsive levels of pentylenetetrazol (Metrazol) photic stimulation induced an augmented rhythmic sequence of late neuron population burst inhibition periods in the dorsal LGN. This late bursting inhibition activity was associated with the augmentation of cortically recorded photically evoked afterdischarges (PhADs). MUA was also recorded from superior colliculus (SC), reticular formation (RF), posterior thalamic area (PTN), and dorsal hippocampus (HIPP). Only SC and FR exhibited an initial discharge to photic stimulation with late bursting infrequently observed and only in the SC. The results are discussed in terms of a recurrent LGN inhibitory system governing cortical PhAD production and elaboration. 28 references. (Author abstract modified)

232325 Neckers, L. M.; Bertilsson, L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The action of fenfluramine and pchloramphetamine on serotonergic mechanisms: a comparative study in rat brain nuclei. (Unpublished paper).** Washington, DC, NIMH, 1975. 12 p.

The action of fenfluramine (F) and p-chloramphetamine (PCA) on serotonergic mechanisms was compared in rat brain

nuclei. A single injection of F or PCA decreased the serotonin (5-HT) content and the tryptophan hydroxylase (TPH) activity in various areas of the rat brain. F fails to reduce the TPH activity in a serotonergic midbrain nuclear (B9). In hippocampus, the decrease of TPH elicited by F persists for less than 21 days; in contrast, PCA reduces the TPH activity in hippocampus, straitum, septal nuclei, and B9 for longer than 21 days. The decrease of TPH elicited by PCA in B9 is attributed to retrograde degeneration; the intensity and duration of the biochemical lesion induced by F and PCA in serotonergic terminals are factors in determining the extent of the biochemical lesion in serotonergic cell models. 13 references. (Author abstract modified)

232328 Le Bars, D.; Menetrey, D.; Conseiller, C.; Besson, J. M. Laboratoire de Physiologie des Centres Nerveux, Universite Pierre et Marie Curie, avenue Gordon-Bennett, Paris, France 75016 **Depressive effects of morphine upon lamina V cells activities in the dorsal horn of the spinal cat.** Brain Research (Amsterdam). 98(2):261-277, 1975.

The effects of morphine upon the transmission of nociceptive messages at the spinal level were investigated in spinal cats by studying the activities of lamina V dorsal horn. Intravenous morphine (2mg/kg) induced a direct depressive action at the spinal level, strongly reducing both spontaneous and evoked activities of lamina V cells. The spontaneous firing rate and the responses elicited by natural nociceptive stimulation were decreased by 50%. The responses of these units evoked by supramaximal electrical stimulation were reduced to 67% of their initial value; in this case, the depressive effect was much more prominent on the late component of the long duration responses. The observed depressive effects are specific since they are immediately reversed by administration of opiate antagonists (nalorphine or naloxone). 53 references. (Author abstract modified)

232333 Blackman, J. G.; Borison, H. L.; Milne, R. J. Dept. of Pharmacology, University of Otago Medical School, Dunedin, New Zealand **Intracellular recording of after-discharge induced by veratrum alkaloids in the guinea-pig nodose ganglion.** Brain Research (Amsterdam). 98(2):369-372, 1975.

The mechanism by which the veratrum alkaloids induce vomiting was examined in albino guinea-pigs. Intracellular recordings from the superficial cells of the nodose ganglion indicate that veratrum alkaloids can produce a long-lasting after-depolarization, often giving rise to trains of action potentials, following direct stimulation through the recording electrode or indirect stimulation through the vagus nerve. They did not cause spontaneous firing. Results are consistent with the view that the veratrum alkaloids may induce vomiting by multiplying normal impulse traffic through the nodose ganglion. 10 references.

232502 Coscia, L.; Causa, P.; Giuliani, E.; Nunziata, A. Research Laboratories, Richardson-Merrell S.p.A., Via P. Castellino 111, I-80100 Naples, Italy **Pharmacological properties of new neuroleptic compounds.** Arzneimittel-Forschung (Aulendorf). 25(9):1436-1442, 1975.

The neuroleptic activity of RMI-61-140, RMI-61-144, and RMI-61-280, which are newly synthesized N-(8-R-dibenzo(b,f) oxepin-10-yl)-N′-methyl-piperazine-maleates, was compared to the neuroleptic activity of chlorpromazine (CPZ) and chlordiazepoxide (CPD). The inhibition of motility observed in mice shows that the compounds reduce the normal spontaneous motility as well as the muscle tone. The central depressant activity is evidenced by increased barbiturate induced sleep; a remarkable eyelid ptosis can also be observed. These compounds do not show any activity on electroshock. As to the antipsychotic outline, these compounds show strong reduction of lethality due to amphetamine in grouped mice and a strong antiapomorphine activity. They also show an antiaggressive effect and an inhibitory activity on avoidance behavior much stronger than CPZ. Extrapyramidal effects such as catalepsy were also found. As for vegatative phenomena, the compounds show hypotensive dose related action ranging from moderate to strong, probably due to alpha receptor inhibition. 19 references. (Author abstract modified)

232506 Costa, E.; Greengard, Paul. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Mechanism of action of benzodiazepines.** Advances in Biochemical Psychopharmacology, Vol. 14. New York, Raven Press, 1975. 181 p. $14.50.

A collection of papers summarizing recent research in the mechanism of action of benzodiazepines (BZP) is presented. Topics considered include: behavioral analysis of the action of BZP; effects of BZP on central serotonergic mechanisms; the involvement of gamma-aminobutyric acid mechanisms in the action of BZP on central catecholamine neurons, on rat cerebellum, and on bullfrog sympathetic ganglia; action of BZP on the cholinergic system; the role of central glycine receptors in the action of BZP; and electrophysiological analysis of the site of action of BZP.

232507 Fuxe, Kjell; Agnati, Luigi F.; Bolme, Per; Hokfelt, Tomas; Lidbrink, Peter; Ljungdahl, Ake; Perez de la Mora, Miguel; Ogren, Sven-Ove. Dept. of Histology, Karolinska Institutet, Stockholm, Sweden **The possible involvement of GABA mechanisms in the action of benzodiazepines on central catecholamine neurons.** In: Costa, E., Mechanism of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 45-61).

The action of chlordiazepoxide, diazepam, and nitrazepam in reducing telencephalic dopamine (DA) turnover and cortical norepinephrine (NE) turnover and counteracting stress induced increases in NE turnover in most parts of the brain was investigated using quantitative microspectrofluorometry. Changes in limbic DA turnover were observed at doses close to the minimal effective dose needed to release punished behavior and to cause anticonvulsant effects and may therefore be related to these actions of diazepam. It is speculated that an increased gamma-aminobutyric acid (GABA) receptor activity on the DA cell bodies and their dendrites is involved in the reduction of DA turnover observed after benzodiazepines, by diminishing the firing rate in the ascending DA pathways, particularly the mesolimbic pathways. It is suggested that the reduction of cortical NE turnover and the corresponding sedative effect found after benzodiazepines may involve increased GABA receptor activity on locus ceruleus cells. The increase in NE turnover elicited by yohimbine, a drug which induces anxiety in man, was blocked by diazepam, a finding consistent with the view that the antianxiety effects of the benzodiazepines are related to blockade of stress induced increases of NE turnover. 41 references.

232508 Stein, Larry; Wise, C. David; Belluzzi, James D. Wyeth Laboratories, Philadelphia, PA 19101 **Effects of benzodiazepines on central serotonergic mechanismss.** In: Costa, E., Mechanisms of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 29-44).

The relation of the behavioral effects of the benzodiazepines and related tranquilizers (barbiturates, meprobamate) to their

effects on monoamine turnover in the brain is considered. Evidence which suggests that tranquilizers may exert their antianxiety effects at least in part by a reduction in central serotonin activity and their depressant effects by a reduction in central norepinephrine activity is reviewed. Preliminary tests in rats which indicate that benzodiazepines may influence monoamine turnover by secondary effects which arise from a primary action on gamma-aminobutyric acid (GABA) are reported: administration of the GABA antagonist picrotoxin fully antagonized the anxiety reducing effects of benzodiazepines in the conflict test. It is concluded that while central serotonin neurons are implicated in the therapeutic actions of benzodiazepines, the drugs may be acting indirectly, via the GABA-ergic systems, to reduce serotonin activity. 33 references.

232510 Consolo, S.; Garattini, S.; Ladinsky, H. Istituto de di Ricerche Farmacologiche "Mario Negri", Via Eritrea, 62-20157 Milan **Action of the benzodiazepines on the cholinergic system.** In: Costa, E., Mechanisms of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 63-80).

The role of the cholinergic system in the action of benzodiazepines was investigated in rats, mice, and guinea-pigs. Results indicate that the effect of diazepam on brain acetycholine (ACh) is specific, as the steady state levels of other amines (histamine, serotonin, norepinephrine, and dopamine) and their metabolites were unaltered by this drug treatment. However, the benzodiazepines decreased norepinephrine turnover in some specific brain areas and dopamine turnover in the corpus striatum. The action of diazepam in increasing ACh levels was limited to the hemispheric structures in all three species considered; this biochemical localization of action is in agreement with electrophysiological data which has focused the action of diazepam on the limbic system, particularly on the amygdala and hippocampus. Since the increase in brain ACh is accompanied by a lack of effect on choline levels, choline acetyltransferase, and cholinesterease activities, it is suggested that diazepam may act centrally by blocking the release of ACh from preganglionic nerve terminals. Possible indirect or secondary mechanisms for the hemispheric increase of ACh after diazepam are outlined. 55 references.

232511 Synder, Solomon H.; Enna, S. J. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **The role of central glycine receptors in the pharmacologic actions of benzodiazepines.** In: Costa, E., Mechanisms of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 81-91).

To investigate the role of central glycine receptors in the pharmacological action of benzodiazepines, the binding of radiolabeled strychnine, a potent glycine antagonist, to synaptic membrane preparations of spinal cord and brainstem was measured as a means of specifically labeling glycine receptors. The relative potencies of 21 benzodiazepines in inhibiting strychnine binding was found to correlate very closely with their potencies in human biossay, based on the minimal dose at which 50% of the subjects experience subjective effects. As there is no correlation between the lipid solubilities of the 21 drugs used and their ability to displace strychnine binding, it is suggested that ability to penetrate lipid barriers is not a determining factor in their apparent affinity for the glycine receptor. It is concluded that the available evidence is consistent with the hypothesis that benzodiazepines exert their antianxiety and muscle relaxing effects by mimicking glycine at its receptor sites. 21 references.

232512 Padjen, Ante; Bloom, Floyd. Laboratory of Neuropharmacology, Division of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Problems in the electrophysiological analysis of the site of action of benzodiazepines.** In: Costa, E., Mechanism of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 93-102).

Electrophysiological data on the analysis of actions of benzodiazepines with both microelectrodes and macroelectrodes are examined in an attempt to integrate these data into testable hypotheses of electrophysiological effects. Methodological difficulties which impede the assessment of cortical effects are considered, and it is noted that microiontophoresis, usually the most appropriate technique for the assessment of potential transmitter agonists or antagonists, is rarely used with the benzodiazepines because of their poor solubility. Studies of both the cortex and the spinal cord have suggested that, through several neurotransmitter systems, the benzodiazepines suppress the extension of sensory information from the primary sensory system into the more associative sensory systems. Evidence implicating gamma-aminobutyric acid (GABA) in the mechanism of action for benzodiazepines is reviewed, a GABA mediation hypothesis is outlined, and suggestions for further research in this area are given. 48 references.

232513 Suria, Amin; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Evidence for GABA involvement in the action of diazepam on presynaptic nerve terminals in bullfrog sympathetic ganglia.** In: Costa, E., Mechanism of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 103-112).

In a study of the role of gamma-aminobutyric acid (GABA) in the action of diazepam on presynaptic nerve terminals, it was hypothesized that the inhibition of the posttetanic potential by diazepam and 3′,5′-guanosine monophosphate (cyclic-GMP), in bullfrog sympathetic ganglia is mediated by the release of GABA, which in turn reduces the amount of transmitter released by depolarizing the preganglionic nerve terminals. Results are in agreement with previous research which indicates that the depolarization of nerve terminals elicited by diazepam and/or cyclic-GMP in bullfrog sympathetic ganglia may depend on the release of GABA located in the glial cells present in this ganglion. Diazepam, cyclic-GMP, and GABA depolarize the terminals of preganglionic axons without decreasing the membrane potential of the interganglionic nerve axons. The depolarization exerted by these compounds can be blocked by picrotoxin. If GABA synthesis is inhibited by isoniazid or thiosemicarbazid, the presynaptic membrane depolarization elicited by diazepam and cyclic GMP is abolished, but GABA retains its action. 33 references.

232514 Costa, E.; Guidotti, A.; Mao, C. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Evidence for involvement of GABA in the action of benzodiazepines: studies on rat cerebellum.** In: Costa, E., Mechanisms of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 113-130).

Experiments in rats designed to test the hypothesis that gamma-aminobutyric acid (GABA) participates in the mediation of diazepam action in the cerebellum are summarized. GABA released at the level of the inhibitory synapses impinging upon Purkinje cells decreases the cerebellar cGMP (cyclic 3′5′-guanosine monophosphate) content. A decrease of GABA-ergic function elicited by either GABA synthesis inhibition

(isoniazid) or the blockade of GABA receptors (picrotoxin) produces a large increase of cerebellar cGMP content without changing the cAMP content. The increase of cerebellar cGMP content caused by harmaline, isoniazid, and picrotoxin is reduced or blocked by small doses of diazepam. The selectivity and high potency of diazepam and other benzodiazepines in antagonizing the biochemical and behavioral effects of isoniazid suggest a participation of GABA-ergic mechanisms in the pharmacological and therapeutical actions of benzodiazepines. 40 references.

232515 Haefely, W.; Kulcsar, A.; Mohler, H.; Pieri, L.; Polc, P.; Schaffner, R. Dept. of Experimental Medicine, F. Hoffman-La Roche & Co. Ltd., Basel, Switzerland **Possible involvement of GABA in the central actions of benzodiazepines.** In: Costa, E., Mechanism of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 131-151).

The effects of several benzodiazepines on a variety of nervous activities known or presumed to depend on gamma-aminobutyric acid (GABA) are presented and compared with those of agents that deplete or increase the level of endogenous GABA: antagonisms of various convulsant agents in mice, enhancement of presynaptic inhibition in the spinal cord and the cuneate nucleus of cats, decrease of the spontaneous firing rate of cerebellar Purkinje cells in cats and rats, antagonism of bicuculline induced depression of the nigrostriatal evoked potential in the cat, potentiation of haloperidol induced catalepsy in rats, and GABA mimetic actions on eserine induced circling in guinea-pigs. Diazepam slightly increased the GABA level in the cat spinal cord and in the total brain of mice and rats. It is concluded that benzodiazepines probably enhance presynaptic inhibition at all levels of the neuraxis and that this effect requires not only the presence of GABA but is also dependent on an activity of GABA-ergic neurons. Benzodiazepines also appear to enhance postsynaptic inhibition where this is mediated by GABA. 39 references. (Author abstract modified)

232516 Hess, S. M.; Chasin, M.; Free, C. A.; Harris, D. N. Squibb Institute for Medical Research, Princeton, NJ 08540 **Modulators of cyclic AMP systems.** In: Costa, E., Mechanism of actions of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 153-167).

Experiments are reported which examined the effects of various therapeutic agents on the activity and metabolism of cyclic 3',5'-adenosine monophosphate (cAMP). Results indicate that agents which act as inhibitors of phosphodiesterase (PDE) in cell free systems exert their influence on cAMP in tissue slices of the brain of guinea-pigs by mechanisms that do not seem to be related to an effect on PDE. Papaverine, and possibly chlordiazepoxide, may act by releasing agonists that in turn stimulate the accumulation of cAMP. This activity is blocked by other inhibitors of PDE, such as theophylline. It is concluded that although many centrally acting agents are modulators of cAMP, it is difficult to establish a direct connection between the pharmacologic activity and levels of cAMP in the brain. 32 references.

04 MECHANISM OF ACTION: BEHAVIORAL

225569 Cutler, Margaret G.; Mackintosh, John H.; Chance, Michael R. A. University of Birmingham, Birmingham 15, UK **Effects of cannabis resin on social behaviour in the laboratory mouse.** Psychopharmacologia (Berlin). 41(3):271-276, 1975.

The effects of cannabis resin on social behavior were studied by an ethological analysis of encounters between male mice injected with the drug and partners injected with Tween saline. The duration of immobility was directly related to the logarithm of the dose of cannabis given. The ratio of flight in treated animals to aggression in mice with which they were paired showed a progressive increase as the dose was raised. A straight line relationship was found to exist between the logarithm of flight aggression and the logarithm of the dose. Nonsocial activity and social investigation were decreased by the administration of cannabis due to the time spent by treated animals in immobility. Aggression was not significantly altered. 17 references. (Author abstract modified)

225571 Desmedt, L. K. C.; van Bruggen, J. A. A.; Niemegeers, C. J. E. Janssen Pharmaceutica, Research Laboratoria, B-2340 Beerse, Belgium **The effects of azaperone, a sedative neuroleptic of the butyrophenone series, on dominant-subordinate behaviour in Wistar rats competing for food.** Psychopharmacologia (Berlin). 41(3):285-289, 1975.

The effects of azaperone, a sedative neuroleptic of the butyrophenone series with antiaggressive and antishock activity, on dominant/subordinate relationship in pairs of rats competing for food are described. In treating the dominant rat of a pair with azaperone, a dose related weakening (at 0.16 and 0.31 mg/kg) reversal (at 0.63 mk/kg and above) of the initial strong dominant/subordinate relationship was demonstrated. Dominant/subordinate relationships were modified by azaperone at doses far below those inducing gross behavioral changes. Results suggest that azaperone has a normalizing effect on social interaction through inhibition of aggressive responsiveness. 7 references. (Author abstract modified)

225573 Smith, Donald F. Psychiatric Hospital, Aarhus University, DK-8240 Risskov, Denmark **Biogenic amines and the effect of short term lithium administration on open field activity in rats.** Psychopharmacologia (Berlin). 41(3):295-300, 1975.

Experiments were performed to examine whether the effects of short-term lithium administration on cerebral biogenic amine metabolism might be related to its action on open field activity. Rats intragastrically injected with lithium chloride (1.5meq/kg twice daily for 5 days) decreased exploratory behavior in the open field. Imipramine failed to influence this behavioral effect, but parachlorophenylalanine prevented it. Pargyline counteracted the effect on exploratory behavior and influenced the emotionality of animals in the open field. Findings are considered consistent with the hypothesis that cerebral monoamine levels and monoamine oxidase activity play a role in the effect of short-term lithium administration on open field activity in rats. 28 references. (Author abstract modified)

226185 Zivkovic, Branimir; Guidotti, Alessandro; Costa, Erminio. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **The regulation of the kinetic state of striatal tyrosine hydroxylase and the role of postsynaptic dopamine receptors.** Brain Research (Amsterdam). 92:516-521, 1975.

Experiments are presented to demonstrate that after cerebral hemisection the stimulation or the blockade of dopamine (DA) receptors change the kinetic state of striatal tyrosine hydroxylase (TH) only in the intact side. It is shown that the regulation of the kinetic state of striatalatal TH is unrelated to the function of autoreceptors located at dopaminergic nerve terminals in striatum. The experiments failed to support the theory that an adenylate cyclase sensitive to DA located in dopaminergic axon terminals regulates the kinetic

state of TH in striatum. It is concluded that the postsynaptic DA receptors are involved in the regulation of the kinetic state of stratal TH. 25 references.

226186 Karpiak, Stephen E., Jr.; Rapport, Maurice M. Dept. of Biochemistry, College of Physicians and Surgeons, Columbia Univ., New York, NY 10032 **Behavioral changes in 2-month-old rats following prenatal exposure to antibodies against synaptic membranes.** Brain Research (Amsterdam). 92:405-413, 1975.

Two month old male offspring of rats were injected intravenously on day 19 of gestation with antiserum to synaptic membrane fraction to measure the resulting behavioral changes. Subjects showed marked behavioral deficits on a DRL (differential reinforcement at low rates) training paradigm in the form of perseveration, slow acquisition rates, and poor retention. Offspring of rats injected during pregnancy with antiserum to galactocerebroside or isotonic saline did not show these behavioral effects. These results are seen to extend earlier observations that antibodies against the synaptic membrane fraction are able to alter behavior. 22 references. (Journal abstract modified)

226305 Ellen, Paul; Aitken, William C., Jr.; Sims, Thomas; Stahl, Jeanne M. Department of Psychology, Georgia State University, 33 Gilmer St., S.W., Atlanta, GA 30303 **Cholinergic blockade, septal lesions, and DRL performance in the rat.** Journal of Comparative and Physiological Psychology. 89(5):409-420, 1975.

Four experiments describing the effects of cholinergic blockade produced by systemic injection of either atropine sulfate or atropine methyl nitrate on the differential reinforcement of low rate (DRL) responding of rats are reported. It was shown that atropine sulfate injected either chronically or at high dosages suppressed DRL responding. Injected acutely, atropine sulfate produced disinhibitory effects. When atropine was injected either chronically or acutely into animals with septal lesions, there was suppression of responding. It is suggested that the specific behavioral outcome resulting from cholinergic blockade depends on the balance resulting from the competing peripheral and central effects of such blockade. 27 references. (Journal abstract)

226405 Baldessarini, Ross J.; Amatruda, Thomas T., III; Griffith, Fred F.; Gerson, Sylvia. Psychiatric Research Laboratories, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114 **Differential effects of serotonin on turning and stereotypy induced by apomorphine.** Brain Research (Amsterdam). 93(1):158-163, 1975.

Differential effects of serotonin on turning and stereotypy induced by apomorphine are reported. Rats with unilateral nigrostriatal lesions were prepared, and their contralateral circling responses to a low dose of apomorphine was measured. The stereotyped gnawing responses of other intact rats to higher doses of apomorphine following several treatments, which increased or decreased the availability or actions of serotonin in the forebrain, were studied. Results indicate that the two syndromes are pharmacologically dissimilar and that caution should be exercised in drawing conclusions about central functions mediated by dopamine from either of them in isolation. Continued questioning of the general equivalence of the circling and stereotypy syndromes as models of central dopaminergic mechanisms is urged. 28 references.

226528 Middaugh, Lawrence D.; Santos, Carroll A.; Zemp, John W. Department of Biochemistry, Medical University of South Carolina, 80 Barre Street, Charleston, SC 29401 **Effects of phenobarbital given to pregnant mice on behavior of mature offspring** Developmental Psychobiology. 8(4):305-313, 1975.

In a study examining the relation between prenatal phenobarbitol and behavior, mature offspring of Mus musculus mice injected daily with phenobarbital for the last third of pregnancy differed from saline and untreated control animals on three measures of behavior. Offspring of phenobarbital treated animals had higher locomotor scores than controls during an open field activity test at 75 days of age. Male offspring were also tested on a one trial passive avoidance task and treated animals were found to be deficient. Female offspring responded less than controls on fixed ratio schedules of reinforcement. The behavioral changes suggest that offspring of mice injected with phenobarbital during pregnancy are less responsive to the stimuli in their environment which maintain behavior. 21 references. (Author abstract modified)

226532 Chen, Chia-Shong; Fuller, John L. Psychology Department, Monash University, Clayton 3168, Australia **Neonatal thyroxine administration, behavioral maturation, and brain growth in mice of different brain weight.** Developmental Psychobiology. 8(4):355-361, 1975.

To study the effects of neonatal thyroxine administration, L-thyroxine in varying amounts was injected daily from age 5 through 14 days in three lines of mice selected for high (H), medium (M), or low (L) brain weight. Controls (injected with vehicle only) of these lines differed in ages of eye opening, first auditory startle, and perfection of a surface righting response. Thyroxine at 5 mg./day accelerated the maturation of eye opening, auditory startle, and aerial righting response, but had no effect on a grasping response or open field activity. Brain weights were depressed significantly in all thyroxine treated groups except in the 5 mg. dosage in H mice. 12 references. (Author abstract modified)

226729 Glick, Stanley, D.; Cox, Russell, D.; Greenstein, Stuart. Dept. of Pharmacology, Mount Sinai School of Medicine, CUNY, Fifth Ave. and 100th St., New York, NY 10029 **Relationship of rats' spatial preferences to effects of d-amphetamine on timing behavior.** European Journal of Pharmacology (Amsterdam). 33(1):173-182, 1975.

The relationship of rats' spatial preferences to effects of d-amphetamine on timing behavior was studied. Rats were trained to bar-press on a differential reinforcement of low rate 16 sec (DRL 16) schedule for water reinforcement. Rats showed consistent side preferences for left or right levers. Performance under an unsignaled condition was much more sensitive to a d-amphetamine induced rate increment and timing impairment than performance during the signaled condition. With increased drug dosage, under both conditions, side preferences depended upon the particular pattern of paw usage and the relationship between paw and side preferences. For the nonsignaled condition, lower rates and better timing performance were significantly correlated with greater preferences. It is suggested that stereotyped motor patterns associated with side preferences are related to mechanisms involved in timing behavior and perhaps, in behavior controlled by internal stimuli generally. 13 references. (Author abstract modified)

226734 Jacobs, Barry L.; Trimbach, Charles; Eubanks, Edwin E.; Trulson, Michael. Department of Psychology, Princeton University, Princeton, NJ 08540 **Hippocampal mediation of raphe lesion- and PCPA-induced hyperactivity in the rat.** Brain Research (Amsterdam). 94(2):253-261, 1975.

The hypothesis that median raphe lesion or p-chlorophenylalanine (PCPA) induced hyperactivity in the rat is mediated specifically by the hippocampus was tested. Aspiration of the anterodorsal hippocampus of adult male rats prior to median raphe lesions or PCPA administration abolished the ability of both of these treatments to produce locomotor hyperactivity in animals chronically housed in tilt cages. Control lesions of the overlying dorsal cortex and corpus callosum were ineffective in blocking the hyperactivity produced by these two treatments. The possibility that serotonin depletion induced hyperactivity was dependent on the pituitary was excluded by the fact that PCPA effectively elevated the activity of hypophysectomized rats. These data indicate that serotonin depletion induced hyperactivity in the rat is mediated by the hippocampus. 12 references. (Author abstract modified)

226764 Malor, R.; Jackson, D. M.; Chesher, G. B. Department of Pharmacology, University of Sydney, Sydney, N.S.W., 2006, Australia **The effect of delta9-tetrahydrocannabinol, cannabidiol and cannabinol on ether anaesthesia in mice.** Journal of Pharmacy and Pharmacology (London). 27(8):610-612, 1975.

The effect of the pure cannabinoids on ether anesthesia in mice was examined. Delta9-tetrahydrocannabinol (THC) produced a dose dependent prolongation of ether anesthesia. The prolongation of anesthesia produced by cannabinol (CBN) was not dose dependent, and the prolongation was less marked as the dose was increased. In contrast, the effect of cannabidiol (CBD) suggested a reversal of ether anesthesia. At a dose of 20mg/CBD, only 4 of 15 mice tested were anesthetized with ether, and the mean duration of anesthesia of these animals was similar to that of the controls. At the lower dose, CBD was without effect on the duration of anesthesia and the number of mice not anesthetized by ether was similar to that observed in the control group. An investigation of cannabinoid interactions suggested that the effect of combining THC and CBD was no different from the effect of THC alone, and was not antagonistic, whereas the effect of combining CBD with CBN appeared to reverse the effect of CBN. While the interaction between THC and CBN appears to be one of addition, the data suggest that the ability of THC and CBN to prolong ether anesthesia may be mediated by different mechanisms. 10 references.

226852 Bond, N. W.; Sanger, D. J.; Blackman, D. E. School of Behavioural Sciences, Macquarie University, Macquarie, Australia **Effects of d-amphetamine on the behavior of pigeons maintained by a second-order schedule of reinforcement.** Journal of Pharmacology and Experimental Therapeutics. 194(2):327-331, 1975.

The effects of various doses of d-amphetamine were studied on the responding of two pigeons exposed to a second order schedule of reinforcement. With this schedule, food was presented following the completion of a sequence of three 2 minute fixed-interval components. A visual stimulus was presented at the completion of each fixed-interval, including the one which was terminated with food. The pigeons' behavior was characterized by a pause immediately after each stimulus presentation followed by a gradual increase in response rate as the interval progressed. d-Amphetamine was found to increase the low rates of responding which occurred early in each interval and to decrease the high rates of responding at the end of each interval. These effects occurred whether responding preceded the presentation of food or the brief stimulus alone. 18 references. (Author abstract)

226853 MacPhail, Robert C.; Gollub, Lewis R. Department of Pharmacological and Physiological Sciences, University of Chicago, 947 E. 58th St., Chicago, IL 60637 **Separating the effects of response rate and reinforcement frequency in the rate-dependent effects of amphetamine and scopolamine on the schedule-controlled performance of rats and pigeons.** Journal of Pharmacology and Experimental Therapeutics. 194(2):332-342, 1975.

The effects of response rate and reinforcement frequency on the rate dependent effects of amphetamine and scopolamine were examined in the rat and pigeon. With rats, the lowest response rate was associated with a higher reinforcement frequency. The effects of d-amphetamine in rats and pigeons were closely associated with the dose, and with the response rates that occurred under nondrug control conditions. Small doses of d-amphetamine increased low response rates proportionately more than moderate rates; moderate rates were increased proportionately more than were high rates. With larger doses, low rates were decreased proportionately less than were moderate rates, which in turn were decreased proportionately less than were high rates. Similar relations between drug effects and control rates were obtained in rats with scopolamine with the exception that constant effects appeared at doses of 0.1mg and greater. Results show that the rate dependent effects of d-amphetamine and scopolamine are primarily response rate dependent drug effects. 41 references. (Author abstract modified)

226854 Sanger, D. J.; Blackman, D. E. Department of Psychology, University of Birmingham, P.O. Box 363 Birmingham, Bl5 2TT, England **Rate-dependent effects of drugs on the variable-interval behavior of rats.** Journal of Pharmacology and Experimental Therapeutics. 194(2):343-350, 1975.

The rate dependent effects of drugs on the variable-interval (VI) behavior of rats were examined. Three rats were exposed to a VI schedule of food reinforcement and three were exposed to the same VI schedule but with the added constraint that reinforcement could follow only a response which occurred at least 5 seconds after the preceding response. The rats exposed to this pacing requirement responded at considerably lower rates, but obtained only slightly fewer reinforcers than those exposed to the simple VI schedule. The effects of d-amphetamine were found to be dependent on the schedule which maintained behavior. This drug produced a dose related decrease in rates of responding maintained by the unpaced VI schedule but a dose related increase in the much lower rates maintained by the pace VI schedule. The effects of chlordiazepoxide were not so clearly schedule dependent although there were some differences between the effects of this drug on responding maintained by the two schedules. These results support the view that the effects of d-amphetamine depend critically on the rate of the response under investigation, but this does not appear to be the case for chlordiazepoxide. 35 references. (Author abstract)

226874 Goldman, Harold; Dagirmanjian Rose; Drew, William G.; Murphy, Sharon. Dept. of Pharmacology, Wayne State Univ. School of Medicine, Detroit, MI 48201 **Delta9-tetrahydrocannabinol alters flow of blood to subcortical areas of the conscious rat brain.** Life Sciences (Oxford). 17(3):477-482, 1975.

The regional perfusion of the nervous systems of conscious, unrestrained rats were examined after the administration of delta9-tetrahydrocannabinol (THC). THC induced cataleptoid postures, vocalization, and in about half of the animals, a unique jumping behavior. During the period of cataleptoid

behavior at 20 minutes after injection, the flows of blood to dorsal hippocampus, hypothalamus, cerebellum and basal ganglia were reduced significantly, whereas perfusion of cortical areas was unaffected. These regional changes in flow are believed to reflect acute functional responses to THC. 38 references. (Author abstract)

226926 Richards, R. K. Department of Anesthesia, Stanford University Medical Center, Palo Alto, CA 94305 **A study of the effect of d-amphetamine on the toxicity, analgesic potency and swimming impairment caused by potent analgesics in mice.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 216(2):225-245, 1975.

The toxicity, analgesic potency and degree of physical impairment (swimming endurance) of a combination of 12mg morphine sulfate with 10mg d-amphetamine HCl per ml were examined in mice. Meperidine, methadone and pentazocine were substituted for morphine using clinically equally analgesic doses and keeping the d-amphetamine amount constant. The toxicity of all analgesics, especially that of morphine, was enhanced in the combination, least so in the case of meperidine. The degree of increase of analgesic power by the addition of d-amphetamine was greatest with morphine and quantitatively in satisfactory agreement with present clinical experiences. Swimming endurance was decreased with full analgesic doses of all four compounds. The presence of d-amphetamine tended to reverse this depression. The data were analyzed in relation to their possible predictive value for the use of such combinations in man for the therapeutic dose range and in the event of overdosage. 31 references. (Author abstract modified)

226932 Inoue, Naohide; Tsukada, Yasuo; Barbeau, Andre. Department of Neurobiology, Clinical Research Insitute of Montreal, Montreal, Canada **Behavioral effects in rats following intrastriatal microinjection of manganese.** Brain Research (Amsterdam). 95(1):103-124, 1975.

The behavioral effects in rats were examined following intrastriatal microinjection of manganese. The injection of manganese into one caudate nucleus in rats resulted in a predominant ipsilateral turning behavior, accompanied at higher doses by an intermittent, alternating and dose realted incidence of contralteral turning and stereotypies. Tegmental serotoninergic and intrastriatal cholinergic pathways appear to be involved in the production of the basic postural asymmetry resulting in turning. The amount of interference with the nigrostriatal and mesolimbic dopaminergic pathways may determine the speed of circling, and the concurrent inhibition of locomotion. This is more evident with bilateral injections. Manganese appears to act at presynaptic levels within the striatum by blocking release of the transmitter, thus creating a localized, relative deficit in caudate function. The end result is the relase of the dominant ipsilateral syndrome inducing system from its inhibitory control. 91 references.

226937 Kelly, Peter H.; Seviour, Paul W.; Iversen, Susan D. Department of Experimental Psychology, Downing Street, Cambridge, England **Amphetamine and apomorphine responses in the rat following 6-OHDA lesions of the nucleus accumbens septi and corpus striatum.** Brain Research (Amsterdam). 94(3):507-522, 1975.

In a study of amphetamine and apomorphine responses in the rat, 6-hydroxydopamine (6-OHDA) injected bilaterally into the nucelus accumbens septi (NAS) or the caudate nucleus of the rat resulted in 79% and 50% depletion of endogenous dopamine (DA) at these respective sites. Fourteen days after the injection a low dose of amphetamine failed to induce the characteristic locomotor response in the NAS lesioned rats but did so in the caudate lesioned animals. By contrast the caudate lesion, but not the NAS lesion, abolished intense forms of stereotyped behavior induced by higher doses of amphetamine. Both lesioned groups exhibited supersensitivity to the dopamine agonist, apomorphine; the NAS group showed enhanced locomotor activity and the caudate group enhanced stereotyped behavior. The block of amphetamine locomotion and the enhanced response to apomorphine were maximal around 14 days after the operation and gradually attenuated up to 90 days. There is evidence that remaining DA levels in the NAS are greater at 90 than at 14 days postoperatively. Thus recovery of behavioral effects correlated with an increase in the remaining levels of DA in the NAS. 35 references. (Author abstract)

226938 Myers, R. D. Laboratory of Neuropsychology, Purdue University, Lafayette, IN 47907 **Impairment of thermoregulation, food and water intakes in the rat after hypothalamic injections of 5,6-dihydroxytryptamine.** Brain Research (Amsterdam). 94(3):491-506, 1975.

The impairment of thermoregulation, food and water intakes in the rat after hypothalamic injections of 5,6-dihydroxytryptamine (5,6-DHT) is described. A bilateral microinjection into the anterior hypothalamus of 5,6-DHT, a substance that lesions serotonin (5-HT) containing neurons, caused a rise in the body temperature of the rat. The anatomical sites were the same as those at which 5-HT given in the same dose range evoked a similar hyperthermia. When exposed for one hour to a temperature of either 35 degrees C or 8 degrees C, the rats were not able to defend against the heat or cold. The magnitude of this thermoregulatory deficit was dependent upon the dose of 5,6-DHT given as well as the site of injection. A partial recovery from the warmth deficit was evident 13-17 days following the 5,6-DHT microinjection. Food and water intakes were also suppressed significantly and bodyweights declined concomitantly. These results provide additional evidence to support the view that a serotonergic mechanism in the hypothalamus is involved in both thermoregulation and the control of ingestive behavior. 44 references. (Author abstract)

226943 Bailey, Paul T.; Pradhan, S. N. Dept. of Pharmacology, Howard University College of Medicine, Washington, DC 20059 **Interactions of adrenergic stimulants and blockers on self-stimualtion behavior in rats.** Research Communications in Chemical Pathology and Pharmacology. 11(4):543-552, 1975.

The interactions of adrenergic stimulants and blockers on self-stimulation behavior were examined in rats. Self-stimulation was facilitated by two adrenergic stimulants, amphetamine and cocaine. Three alpha-adrenergic blockers (phenoxybenzamine, dibenamine, phentolamine) and a belta-adrenergic blocker (propranolol) decreased self-stimulation responding at high i.v. doses but showed very little effect at small i.p. doses. Pretreatment with alpha-adrenergic and beta-adrenergic blockers also decreased amphetamine facilitated responding. The effects of amphetamine or cocaine (i.p.)were not significantly altered by these blockers at the doses used. The depressant effects of the alpha-adrenergic and beta-adrenergic blockers on self-stimulation behavior appear to be non-specific with respect to the type of adrenergic receptors. 14 references. (Author abstract)

226945 Stratten, Wilford P. Department of Physiology, Bowman Gray School of Medicine, Winston-Salem, NC 27103 **Methadone interaction with apomorphine- and amphetamine-in-**

duced turning. Research Communications in Chemical Pathology and Pharmacology. 11(4):675-678, 1975.

The influence of methadone alone and in combination with apomorphine or amphetamine on turning behavior was examined in rats having unilateral nigrostriatal lesions. The apomorphine elicited turning behavior contralateral to the side of the lesion, and amphetamine induced ipsilateral turning. Methadone elicited no turning behavior when administered alone. In two runs of six animals each, methadone, given as a 2 hour pretreatment, significantly reduced contralateral turning induced by apomorphine. This would be expected if methaone were a dopamine receptor blocker. In the same number of animals, however, it was found that methadone does not inhibit turning induced by amphetamine. In fact methadone tended to increase amphetamine induced turning, although the increase was not significant. These findings are interpreted as evidence that, at least following acute methadone treatment, there is an amphetamine induced turning in rats with unilateral nigrostriatal lesions which is not mediated by dopamine. 11 references.

226992 Zabik, Joseph E. University of Rhode Island **Operant analysis of behavior associated with oral self-administration of drug solutions in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-17868 HC$13.50 MF$5.00 337 p.

A method suitable for quantitatively and reliably measuring oral self-administration of drugs and their effects on behavior in experimental animals was developed. Water deprived rats were trained to lick for drug solutions and barpress for food on a fixed-interval (FI) schedule and to press another bar for secondary reinforcement on a fixed-ratio (FR) schedule as three concurrent operants. Results indicate that nondiscriminated responding was inconsequential. An appropriate drug solution was substituted for water, or the drugs were injected intraperitoneally before the session. For each of five drugs (amphetamine, chlorpromazine, ethanol, disulfiram, and morphine) a dose response was determined, usually with six replicate sessions per dose for each of three rats. (Journal abstract modified)

227074 Burge, Katherine Gravelle Emory University **Olfactory bulb removal in mice: activity levels and responsiveness to the locomotor stimulant and anorexic properties of d-amphetamine sulfate. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-16851 HC$13.50 MF$5.00 73 p.

The effects of olfactory bulb removal in female Swiss-Webster mice were studied, and a striking increase in locomotor activity remained evident even 2.5months after surgery. Results indicate that food deprivation increased the motor activity of bulbectomized and sham operated Ss, but the former did not potentiate food deprivation induced hyperactivity. Administration of d-amphetamine sulfate resulted in a dose dependent increase in locomotor activity, but bilateral bulbectomy did not potentiate amphetamine's motor stimulant effect. Results of further experimentation reveal that bulbectomy does not cause a persistent anorexia, but, rather, may disrupt the normal feeding patterns. The determination of the precise manner in which bilateral bulbectomy affects feeding behavior is open for futher research. Although the neurophysiological mechanisms underlying the profound behavioral disruptions caused by the surgery remain to be determined, it is clear that these changes are not exclusively manifested in social behaviors, but also affect such fundamental nonsocial behaviors as locomotor activity and feeding behavior. (Journal abstract modified)

227099 Williams, John Marion. Rutgers University **Disinhibitory effects of septal lesions and scopolamine hydrobromide. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-17481 HC$13.50 MF$5.00 76 p.

The disinhibitory effects of septal lesions and scopolamine hydrobromide on responding were investigated in a series of experiments with laboratory animals. Findings indicate that while exploration of a novel environment and the startle response both wane as a function of time, such habituation is not related to a common process. Results show that injections of scopolamine, but not methyl scopolamine, interfere with habituation of exploration, but have no effect on habituation of the startle response. Medical septal lesions interfered with habituation of both startle and exploration behavior. Also, habituation of startle occurred at a much earlier age than habituation of exploration. Finally, there was an anatomical separation of control of these two types of response. Compared to medial septal lesions, lesions of the entire septum greatly decreased exploration while having little effect on startle. (Journal abstract modified)

227106 Brophy, Patrick Dennis. Southern Illinois University **Angiotensin-induced drinking in the cat: a dose-response and biochemical analysis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-16261 HC$13.50 MF$5.00 110 p.

The intracranial injection of angiotensin amide, in doses of 125-4,000ng injected into the diencephalon of the cat, was found to elicit copious drinking. Drinking responses were of short latency and duration. Volumes of water consumed within 30 min of intracranial injection of 1,000ng angiotensin amide approximated volumes consumed after 25 hr of water deprivation. A definite dose - response relationship occurred, with 1,000ng being an optimum dose. In a second experiment, the enzyme renin was found to elicit drinking in the cat in doses between 1 and 45 Goldblatt mu intracranially injected. A third experiment examined the effects of norepinephrine, dopamine, epinephrine, serotonin, carbachol, and isoproterenol at angiotensin positive sites. A single dose (10 micrograms) of these agents was used, and water intake was unaffected. Sham rage and occasional changes in motor behavior were observed following the intracranial injection of carbachol. (Journal abstract modified)

227125 Stricker, Edward M.; Friedman, Mark I.; Zigmond, Michael J. Psychobiology Program, Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Glucoregulatory feeding by rats after intraventricular 6-hydroxydopamine or lateral hypothalamic lesions.** Science. 189(4206):895-897, 1975.

The effects of intraventricular 6-hydroxydopamine or bilateral electrolytic lesions of the lateral hypothalamus on feeding responses of rats were studied. Normal increase in food intake was not shown in responses to large decreases in glucose utilization or exposure to severe cold stress. However, findings indicate that rats will eat more during chronic glucoprivation that is less intense, or during exposure to moderate cold stress. Thus, the feeding deficits of these lesioned rats may not reflect an inability to respond to certain qualitatively different stimuli, but rather an inability to respond to quantitively different intensities of the same stimulus. 16 references. (Author abstract modified)

227126 Davis, Michael; Svenson, Torgny H.; Aghajanian, George K. Department of Psychiatry, Yale University School

of Medicine, New Haven, CT 06508 **Effects of d- and l-amphetamine on habituation and sensitization of the acoustic startle response in rats.** Psychopharmacologia (Berlin). 43(1):1-11, 1975.

The effects of 2, 4, 8, or 16mg/kg d-amphetamine and 4, 8, 16, or 32mg/kg l-amphetamine on acoustic startle amplitude in the rat were investigated. d-Amphetamine was 4-5 times as potent as l-amphetamine in augmenting startle amplitude. Startle potentiation was associated with vigorous stereotypies but the resultant cage movement could not account for the change in startle. Pretreatment with alpha-methyl-p-tyrosine had only a slight depressant effect on startle but essentially eliminated augmentation of startle by either d-amphetamine or l-amphetamine. d-Amphetamine did not have a direct effect on startle but instead enhanced sensitization produced by the startle stimuli without altering sensitization produced by background white noise or habituation. The results suggest that startle sensitization is enhanced by increased availability of catecholamines and, by virtue of the different potencies of the d and l isomers, that dopamine and norepinephrine may affect startle differently. 61 references. (AUthor abstract)

227127 Downs, David A.; Woods, James H. Department of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Food- and drug-reinforced responding: effects of DITA and d-amphetamine.** Psychopharmacologia (Berlin). 43(1):13-17, 1975.

In a study of food and drug reinforced responding, i.v. pretreatment with DITA; (3',4'-dichloro-2-(2-imidazolin-2-ylthio)-, acetophenone hydrobromide decreased the rate of food reinforced lever pressing in rhesus monkeys. Response rate decreases were dose dependent but showed the development of tolerance. Self-administration of DITA was initiated and maintained in each of three monkeys when 30 lever presses were required to produce each injection. Response rate in periods of food availability immediately preceding drug periods was relatively constant across sessions; response rate in periods of food availability immediately following drug periods, however, decreased with increasing amounts of drug self-administered. Replication of initial self-administration doses produced results comparable to original determinations in contrast to the tolerance observed with DITA effects upon food reinforced responding. DITA was about three times less potent than d-amphetamine in maintaining response rates in drug periods and in decreasing the rate of subsequent food reinforced responding. 7 references. (Author abstract modified)

227128 Meisch, Richard A.; Beardsley, Patrick. Psychiatry Research Unit, University of Minnesota, Box 392 Mayo Memorial Building, Minneapolis, MN 55455 **Ethanol as a reinforcer for rats: effects of concurrent access to water and alternate positions of water and ethanol.** Psychopharmacolgia (Berlin). 43(1):19-23, 1975.

In a study of ethanol as a reinforcer, water and ethanol solutions were concurrently made available on a continuous reinforcement schedule to four food deprived male albino rats during daily 1 hr sessions in an operant conditioning chamber equipped with two levers and two liquid dippers. The number of ethanol reinforcements substantially exceeded the number of water reinforcements for each rat at each concentration studied. Water reinforcements were low in number and did not vary with ethanol concentration. As the ethanol concentration was increased, the number of ethanol reinforcements obtained decreased, while the quantity consumed increased. The highest rate of responding occurred at the beginning of the session. 11 references. (Author abstract)

227129 Lassen, J. Buus. Department of Pharmacology, A/S Ferrosan, Soborg, Denmark **Inhibition of 4,alpha-dimethyl-M-tyramine (H 77/77)-induced hypermobility in rats by single and repeated administration of chlorpromazine haloperidol, clozapine and thioridazine.** Psychopharmacologia (Berlin). 43(1):25-29, 1975.

The effect of H-77/77 (4,alpha-dimethyl-m-tyramine) on motility of rats kept in a familiar cage was investigated. H-77/77 produced hypermotility, which was reduced by oral pretreatment with chlorpromazine, haloperidol, clozapine and thioridazine. The four neuroleptics were administered acutely and for a 14 day period. H-77/77 was given 30 min after the single or last dose of neuroleptic (chronic treatment) condition. The effect on H-77/77 activity did not change significantly after repeated treatment. Clozapine and thioridazine, which clinically produce only minor extrapyramidal side effects, exert a weak effect or none at all in tests commonly used for neuroleptic activity. These two neuroleptics were potent H-77/77 antagonists. Inhibition of H-77/77 hypermotility may possibly be used as test for neuroleptics. 48 references. (Author abstract modified)

227130 Anderson, Pamela F.; Jackson, D. M.; Chesher, G. B.; Malor, R. Department of Pharmacology, University of Sydney, Sydney, Australia **Tolerance to the effects of delta9-tetrahydrocannabinol in mice on intestinal motility, temperature and locomotor activity.** Psychopharmacologia (Berlin). 43(1):31-36, 1975.

The onset and duration of tolerance to three effects of delta9-tetrahydrocannabinol (THC) given orally to mice were compared. The effects of THC studied were: hypothermia, the depression of intestinal motility and the effect on spontaneous locomotor activity. When mice were dosed and tested at 24 hr intervals it was apparent that tolerance was complete to its hypothermic and locomotor depressant effects after the first doses and to depression of intestinal motility after the fourth dose. Duration of tolerance also differed so that the normal hypothermic response had returned after 12 dose free days, but not after 5 drug free days; the effect on locomotor activity had returned within 4 days; and, apparent partial tolerance to the depressant effect of an acute challenging dose of THC on intestinal motility still existed after 19 dose free days. It is apparent that the time of onset and the duration of tolerance to THC in mice showed a different pattern in the three parameters studied. 19 references. (Author abstract modified)

227131 Ksir, Charles. Department of Psychology, University of Wymoning, Laramie, WY 82071 **Scopolamine and amphetamine effects on discrimination: interaction with stimulus control.** Psychopharmacologia (Berlin). 43(1):37-41, 1975.

A parametric examination of the interaction between drug induced behavioral changes and the degree of predrug stimulus control was conducted with rats. A discrete trial simultaneous discrimination was used, with the controlling stimuli varied over six values of distinctiveness. The effects of graded doses of scopolamine, d-amphetamine, and methylscopolamine on these performances were studied, with both scopolamine showing no increase in error rate under strong stimulus control, and dose related increases in error rate under weak stimulus control. The similar interaction between drug effect and stimulus control for scopolamine and d-amphetamine indicates that the interaction reflects the degree of susceptibility of the behaviors to drug action, rather than two specific drug behavior interactions. Methylscopolamine produced a slight effect on error rate and no significant interaction with stimulus control. A decrease in the number of trials responded to was

found with both scopolamine and methylscopolamine, but not with dhamphetamine. 8 references. (Author abstract modified)

227132 Gianutsos, Gerald; Hynes, Martin D.; Drawbaugh, Richard B.; Lal, Harbans. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Paradoxical absence of aggression during naloxone-precipitated morphine withdrawal.** Psychopharmacologia (Berlin). 43(1):43-46, 1975.

In a study of Naloxone preceptitated withdrawal, aggression, which is normally seen during withdrawal from narcotics, could not be produced in morphine dependent rats. Apomorphine injected instead of naloxone was capable of producing aggression, without other withdrawal signs. Naturally occurring aggression 72 hr withdrawal) was enhanced by apomorphine and unaffected by naloxone. 17 references. (Author abstract)

227135 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Detection of the neuroleptic properties of clozapine, sulpiride, and thioridazine.** Psychopharmacologia (Berlin). 43(1):69-74, 1975.

The cataleptic and antistereotypic abilities of clozapine, sulpiride and thioridazine were determined in the rat and compared with the responses of typical neuroleptic agents, haloperidol, fluphenazine and pimozide. Haloperidol and fluphenazine caused a dose dependent cataleptic state which attained maximum intensity: the effects of pimozide were also dose dependent but, although the catalepsy was marked, maximum intensity was not attained. Thioridazine, clozapine and sulpiride each caused a very weak, but definite, cataleptic response although a dose depdency could not be demonstrated. Threshold cataleptic doses of all agents markedly synergised in the production of catalepsy with threshold doses of the cholinergic drug RS86. Similarly, all neuroleptic agents tested were shown to reduce the intensity of the stereotyped behavior induced by amphetamine, apomorphine and nomifensine in a dose dependent manner but only haloperidol, fluphenazine and pimozide were shown to be capable of 100% inhibition. The antistereotypic abilities of haloperidol, fluphenazine and pimozide were most marked against amphetamine, but this was not a consistent observation for thioridazine, clozapine and sulpiride. Threshold, or even subthreshold, doses of both the typical and atypical neuroleptic agents combined with threshold doses of RS86 markedly synergised in the antagonism of the stereotypic actions of amphetamine, apomorphine and nomifensine. 28 references. (Author abstract modified)

227137 Griffiths, Roland R.; Findley, Jack D.; Brady, Joseph V.; Dolan-Gutcher, Karen; Robinson, William W. Department of Psychiatry, John Hopkins University, School of Medicine, Baltimore, MD 21205 **Comparison of progressive-ratio performance maintained by cocaine, methylphenidate and secobarbital.** Psychopharmacologia (Berlin). 43(1):81-83, 1975.

Cocaine, methylphenidate and secobarbital were compared on a drug maintained progressive ratio procedure in baboon subjects. Trials, scheduled throughout the day, occurred at a minimum interval of 3 hrs after completion of the preceding trial. A ratio response requirment on the initate lever was required during each trial which terminated in a single intravenous infusion of drug. A drug was introduced on the progressive ratio procedure with a low ratio requirement in order to obtain a baseline performance of a high stable frequency of trial completion. The ratio requirement was systematically increased every 7 days until the breaking point when the rate of completing trials fell below a criterion level. Within subject comparison revealed that cocaine porduced higher breaking points than methylphenidate at the same absolute dose. At the range of doses studied, manipulation of doses of methylphenidate and cocaine had little effect on breaking point. In contrast, increasing doses of secobarbital produced higher breaking points within the same subjects. 8 references. (Author abstract)

227138 Izquierdo, Ivan; Thaddeu, Roberto. Departamento de Fisologia, Escola Paulista de Medicina, Sao Paulo, Brazil **The effect of adrenaline, tyramine and guanethidine on two-way avoidance conditioning and on pseudoconditioning.** Psychopharmacologia (Berlin). 43(1):85-87, 1975.

The effect of adrenaline, tyramine and guanethiduine on two-way avoidance conditioning and on pseudoconditioning was examined in the rat. Adrenaline or guanethidine given i.p. depressed performance of pseudoconditioned shuttle repsonses by rats. Pretrial administration of any of the three drugs also depressed two way avoidance conditioning. Following postrial administration, only guanethidine had a deleterious effect on retention. Since none of these drugs is believed to reach the brain in significant amounts following systemic injection, the present results suggest that peripheral factors may influence both conditioned and pseudoconditioned shuttle behavior. 16 references. (Author abstract modified)

227385 Van Gelder, G. A.; Cunningham, W. L. Behavioral Toxicology Laboratory, College of Veterinary Medicine, Iowa State University, Ames, IA **The effects of low-level dieldrin exposure on the EEG and learning ability of the squirrel monkey.** Toxicology and Applied Pharmacology. 33(1):142, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williamsburg, Virginia, in March 1973, a paper was presented in which the effects of subclinical exposure on acquisition of a nonspatial successive discrimination reversal task and on onset of dieldrin related electroencephalogram (EEG) alterations in adult male squirrel monkeys were reported. A 0.1mg/kg group achieved significantly fewer reversals than either 0.01 mg/kg or control groups over a 55 day exposure period. Subsequent exposure termination and increase to 0.1mg/kg, for 54 days, did not affect performance in the high and low groups, respectively. The second study recorded four nonexposed EEG's from each of another nine monkeys before exposure began for 60 days at three levels: 0.1mg/kg 0.01 mg/kg and no exposure. High amplitude slow waves occurred more often in the 4 hr recording condition. Most changes occurred on day 50 in both exposure groups. No dieldrin related EEG changes occurred in the control group. Together, continuous daily 0.1mg/kg exposure impaired acquisition and altered the EEG in about the same time frame. Also, continuous exposure at 0.01 mg/kg, below the threshold for enzyme induction altered the EEG. Preliminary date from a third study indicate that 1 yr accumulated 0.01 mg/kg exposure slows acquisition, relative to the rate of acquisition at that level in the first study.

227386 Cohn, M. L. Unviersity of Pittsburgh School of Medicine, Pittsburgh, PA **Acute behavioral changes induced in the rat by the intracerebroventricular administration of thyrotropin releasing factor (TRF) and somatostatin.** Toxicology and Applied Pharmacology. 33(1):142-143, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williamsburg, Virginia, in March 1973, acute behavioral changes induced in the rat by the intracerebroven-

tricular administration of thyrotropin releasing factor (TRF) and somatostatin were reported. Male Sprague-Dawley rats, 80-120 g, intact and thyroidectomized, were injected centrally with TRF and somatostatin TRF (7.50-50 micro g) administered centrally to the unanesthetized rat resulted in intermittent sedation and hyperactivity with tearing, squirrel upright position, arched back, and staggering gait. In intact and thyroidectomized rats, higher concentrations of TRF induced hyperthermia. Combinations of TRF and phentolamine resulted in head-to-tail rotation on a flat surface. The rats were unusually aggressive. In anesthetized rats, TRF shortened the sleeping time but not dose relatedly; the addition of TRF to dibutyryl cyclic 3',5'-adenosine monophosphate further shortened narcosis but with persistent wide ranges of sleeping times. Upon arousal, a severe and acute crerbral locomotor disorder lasting several hours was observed. Lower doses of somatostatin in the nonanesthetized rat resulted in profound sedation and hypothermia. Higher doses induced "barrel rotation."Anesthetized rats slept three to four times longer than the control group. (Journal abstract modified)

227636 Zebrowska-Lupina, Iwona; Malec, Danuta; Kleinrok, Zdzislaw. Zaklad Farmakologii Instytutu Patologii Klinicznej, 20-090 Lublin, Jaczewskiego 8, Poland **Comparison of central effects of noradrenaline and dopamine injected into the lateral brain ventricle in rats.** Acta Physiologica Polonica (Warszawa). 26(3):261-274, 1975.

Noradrenaline and dopamine injected into the lateral brain ventricle exerted a significant effect on the behavior of rats. Both amines caused a slight rise in the basic locomotor activity which was significantly increased in the animals with inhibited monoamine oxidase activity. Besides that, they suppressed the behavior of rats in the open-field test, inhibited the conditioned avoidance response, decreased body temperature and increased amphetamine induced motor hyperactivity. Noradrenaline, in contrast to dopamine, changed the intensity of amphetamine induced stereotypy and prolonged the action of hypnotics. The central action of both catecholamines (in higher doses especially) seemed to have a biphasic course: in the first phase after administration, depression was observed which was more pronounced after noradrenaline administration; in the second phase a stimulating effect became apparent, usually more evident in rats receiving dopamine. 41 references. (Author abstract)

227637 Plech, Andrzej; Drybanski, Andrzej; Herman, Zbigniew S. Zaklad Farmakologii Slaskiej AM, 41-808 Zabrze, Marksa 38, Poland **The effects of neurolopetics and nialamide on defensive conditioned reflex in rats.** Acta Physiologica Polonica (Warszawa). 26(3):255-260, 1975.

The effects of neuroleptics and nialamide on defensive conditioned reflex in rats were investigated. Experiments were carried out on male Wistar rats after development of defensive conditioned reflex during 6 weeks of training. In one series of experiments, chlorpromazine, haloperidol, pimozide or fluspirilene were used in doses of 0.05, 0.5and 5.0mg/kg intraperitoneally. In another series of experiments, nialamide was given intraperitoneally in a dose of 140 mg/kg 16 to 18 hours before administration of one of these neuroleptics. A delay in the time of appearance of the defensive conditioned reflex was observed after administration of neuroleptics in all animals. In some rats, neuroleptics caused complete disappearance of the conditioned reflex as well as the defensive unconditioned reflex. Previous inhibition of monoamine oxidase activity obtained with nialamide increased the inhibitory effect of the neuroleptics on the appearance of defensive conditioned reflex. 21 references. (Author abstract)

227702 Hine, Bromfield; Torrelio, Marina; Gershon, Samuel. Dept. of Psychiatry, New York University School of Medicine, New York, NY **Differential effect of cannabinol and cannabidiol on THC-induced responses during abstinence in morphine-dependent rats.** Research Communications in Chemical Pathology and Pharmacology. 12(1):185-188, 1975.

The differential effect of cannabinol (CBN) and cannabidiol (CBD) on tetrahydrocannabinol (THC) induced abstinence signs and rotational behavior (turning) was examined in morphine dependent rats. The same dose of CBN or CBD further increased the attentuation of precipitated abstinence signs observed in morphine dependent rats that also received an acute dose of delta9-THC. By contrast, rotational behavior, observed concomitantly in THC treated rats during morphine abstinence, was not increased by CBN, but was potentiated by CBD. These data illustrate differences between psychoinactive cannabinoids in their interaction with delta9-THC that might be relevant to possible clinical use of Cannabis in narcotic detoxification. 12 references. (Author abstract modified)

227703 Glick, S. D.; Cox, R. D. Dept. of Pharmacology, Mt. Sinai School of Medicine, CUNY, Fifth Ave. and 100th St., New York, NY 10029 **Dopaminergic and cholinergic influences on morphine self-administration in rats.** Research Communications in Chemical Pathology and Pharmacology. 12(1):17-24, 1975.

In a study of dopaminergic and cholinergic influences on morphine self-administration, various doses of apomorphine, haloperidol, pilocarpine and scopolamine were administered intraperitoneally to rats self-administering intravenous morphine (0.4mg/kg/infusion). Findings indicate that apomorphine, at low doses, increased rates of morphine self-administration and at high doses, decreased these rates. Haloperidol decreased self-administration rates with increasing dose. Both pilocarpine and scopolamine produced only small decreases in rates of self-administration at high doses. When administered in combination, the effects of apomorphine and haloperidol were antagonistic as were the effects of pilocarpine and scopolamine; the effects of apomorphine or haloperidol predominated, however, when either drug was administered in combination with pilocarpine or scopolamine. Results are consistent with previous work implicating an important role for dopaminergic mechanisms in morphine's reinforcing property. 14 references. (Author abstract modified)

227762 Moller Nielsen, Iver. Lundbeck Co., Ottiliavej 7-9, DK-2500, Copenhagen **Pharmacological vs. clinical physiognomy of neuroleptics, with special reference to their sedative and antipsychotic effects.** Acta Psychiatrica Belgica (Bruxelles). 74(5):473-484, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the sedative and antipsychotic effects of neuroleptics in animals were discussed. The best measure of the sedative effect appears to be the inhibition by the drug of the arousal response to electrical stimulation of the midbrain reticular formation. The best model for the antipsychotic effect is obtained by observing the antagonism of the drug to amphetamine or apomorphine induced (in rats) and methylphenidate induced (in mice) stereotyped gnawing. The importance conceptualizing of a drug's action as a dynamic process was stressed.

227763 Dresse, Albert. Department of Pharmacology, University of Liege Medical School, Blvd. de la Constitution 32, B-4000, Liege, Belgium **Biochemical vs clinical physiognomy of neuroleptics, with special reference to their antimanic effect.** Acta Psychiatrica Belgica (Bruxelles). 74(5):485-487, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, two dopaminergic pathways, the A9 nigrostriatal system and the A10 mesolimbic system, which may participate in the antimanic properties of neuroleptics were described. In the nigostriatal system, the parallelisms between antimanic and extrapyramidal scores of neuroleptics in the Liege clinical classification and between degeneration of dopaminergic cell bodies and abatement of thought processes in idiopathic Parkinson patients were stressed. On the other hand, the self-stimulation obtained with electrodes implanted in the mesolimbic system in rats is specifically antagonized by the dopaminergic neuroleptics. The antimanic effect of neuroleptics may be a convergence of dopaminergic effects on motoricity and on mood.

227802 Stoff, David M.; Gillin, J. Christian; Wyatt, Richard J. Clinical Psychopharmacology, NIMH, IRP, St. Elizabeths Hospital, Washington, DC 20032 **5-Methoxy-N,N:dimethyltryptamine (5 MeO-DMT) shares inhibitory effects with mescaline but not excitatory effects on shuttlebox escape/avoidance in rats. (Unpublished paper).** Washington, DC, NIMH, 1975. 1 p.

The behavioral effects of 5-methoxy-N,N:dimethyltryptamine (5-MeO-DMT), a rapidly acting psychedelic agent, and mescaline on acquisition of shuttlebox escape/avoidance were examined in four different strains of rats. Findings indicate that 5-MeO-DMT was ineffective in rats who were poor avoidance performers while mescaline was excitatory in these strains; both agents shared dose response inhibitory effects in rats who were food avoidance performers. These results for 5-MeO-DMT are similar to previous data reported for N,N:dimethyltryptamine (DMT). Neither of the tryptamine derived agents possess excitatory effects on shuttlebox escape/avoidance, contrary to the effects of mescaline and lysergic diethylamide (LSD). All of these drugs share inhibitory effects. If excitatory effects on shuttlebox escape/avoidance are mediated by catecholamines (CA) and inhibitory effects via serotonin, then 5-MeO-DMT and DMT's inability to produce excitation may be related to its lack of effect on CAs, whereas the ability to stimulate serotonergic receptors is shared by 5-MeO-DMT, DMT, LSD and mescaline. 3 references. (Author abstract modified)

228139 Bushnell, Philip J.; Maloff, Perry; Bowman, Robert E. Regional Primate Center, University of Wisconsin, Madison, WI 53706 **Loss of inhibitory motor control following a subanesthetic dose of thiobarbiturate in rhesus monkeys.** Physiological Psychology. 3(3):205-209, 1975.

An operant paradigm was employed to examine the magnitude and duration of the behavioral excitation induced by a subanesthetic dose of a short acting thiobarbiturate drug. Thus, 0.5h following a single intravenous injection of sodium thiamylal (Surital, P.D.;12.5mg/kg), the mean response rate of monkeys previously trained to bar-press for food reinforcement on a variable interval 30 sec schedule was increased threefold. By 3 hours postinjection, drug and saline means were statistically indistinguishable, and by 4 hours, they were virtually identical. Analysis of pauses and interreinforcement response rates from cumulative records showed a tendency for drugged animals to respond in rapid bursts, and undrugged animals to maintain the steady, slow response rate characteristic of performance on a variable interval schedule. Possible central nervous system mediation of this behavioral excitation in terms of interference with inhibitory reticular formation processes is discussed. 15 references. (Author abstract)

228142 Coscina, Donald V.; Goodman, Jeff; Godse, Damodar D.; Stancer, Harvey C. Section of Neurochemistry, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada M5T 1R8 **Effects of handling before central 6-hydroxydopamine treatment on subsequent emotionality and neurochemical changes in rats.** Physiological Psychology. 3(3):225-228, 1975.

Rats were handled daily for 5 minutes 6 days prior to intracisternal 6-hydroxydopamine (6OHDA) treatment to examine a possible ameliorative effect of handling on the rage known to occur after this method of chronic depletion of brain norepinephrine (NE) and dopamine (DA). Handling did not alter the magnitude or time course of the rage; however, it did produce an apparent protective effect against the ability of 6OHDA to deplete brain DA and, possibly, NE. Since previous work has shown that this same handling regimen, instituted after the production of 6OHDA induced rage, has pronounced taming effects, these findings collectively show that handling is a potentially important variable to control in experiments concerned with the behavioral and neurochemical effects of this drug. 10 references. (Author abstract modified)

228143 Davenport, John W.; Hagquist, William W.; Hennies, Richard S. Regional Primate Research Center, University of Wisconsin, Madison, WI 53706 **Neonatal hyperthyroidism: maturational acceleration and learning deficit in triiodothyronine-stimulated rats.** Physiological Psychology. 3(3):231-236, 1975.

In a study of neonatal hyperthyroidism, it was found that rat pups injected on postnatal days 2 to 4 with subcutaneous doses of triiodothyronine (T3) up to 4 micrograms/g showed substantial accelerations in the maturation of swimming behavior, righting reflexes and eye opening which were greater than the accelerations produced by neonatal thyroxine (T4) in a previous study. They also showed significantly higher activity in stabilimeter cages on postnatal day 13 but not an expected earlier peak than normal rats in the ontogeny of arousal functions obtained in stabilimeter testing. As adults, the T3 treated rats displayed large maze learning deficits which were comparable in size to those produced by fairly severe thyroid deficiency in the perinatal period. 19 references. (Author abstract modified)

228160 Bauer, Richard H.; Duncan, Debra L. University of California, Los Angeles, CA 90024 **Differential effects of d-amphetamine in mature and immature rats.** Physiological Psychology. 3(3):312-316, 1975.

The effects of d-amphetamine (d-A) on open-field activity, reactivity to footshock and avoidance learning were compared in mature and immature rats. Sprague Dawley rats (28-33 days old and 120-140 days old) were injected with physiological saline, 2.0or 5.0mg/kg d-A. Thirty minutes after the injection, they explored an open-field for 8 minutes and were then trained in a one-way avoidance task. Mature animals were more active in the inner portion of the open-field following 2.0mg/kg and acquired the avoidance task more rapidly than those given saline or 5.0mg/kg. Neither drug dose altered activity or avoidance of immature animals. Both mature and immature rats had shorter escape latencies to footshock following the drug. Differential effects of d-A in mature and immature animals are probably due to developmental changes in brain norepinephrine and/or dopamine. 22 references. (Author abstract modified)

228390 Wang, Paul Li-cheng. Illinois Institute of Technology **Neurotransmitter influences on mating behavior in male rats.**

(Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-12821 HC$13.50 MF$5.00 108 p.

Neurotransmitter influences in the mating behavior of male copulating and noncopulating Sprague-Dawley rats were examined using acetylcholine, DL-norepinephrine, propranolol hydrochloride, regitine hydrochloride, atropine sulfate, and cinanserin intracranialy implanted into the medial preoptic anterior hypothalamic continuum. Findings indicate that androgen is necessary for the performance of the full copulatory pattern in male rats, and that DL-norepinephrine facilitates mounting behavior in castrated Ss and in noncopulators. In the noncopulators, number of intromissions was also enhanced after DL-norepinephrine treatment. It is suggested that DL-norepinephrine stimulates the male rats and elevates their arousal level, which is responsible for the observed enhancement of mounting frequency. Possible relationships between androgen levels and neurotransmitter effects are also discussed. (Journal abstract modified)

228503 Willard, Stephen Pitts. University of Southern California **Effects of physostigmine on avoidance conditioning and retention in the isolated cockroach ganglion. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-19048 HC$13.50 MF$5.00 149 p.

The effects of physostigmine on avoidance conditioning and retention in the isolated cockroach ganglion were examined to determine if such conditioning can be facilitated by drug induced neural activation and if retention of the response can be enhanced by such activation during the posttraining interval. Three experiments were conducted using physostigmine as the activating agent, and results indicate that both acquisition and retention of a simple avoidance behavior can be facilitated by neural activation. It is hypothesized that such neural activation may also underlie that the apparent facilitative effects of CNS stimulants on learning and memory in higher animals. The consolidation of memory fixation was not directly tested, since the hypothesized time bound nature of that process was not studied. It is tentatively suggested that both amnesic and facilitative agents can produce such effects if applied whenever cues reactivate a significant portion of the total pattern of activity which would occur with a fully expressed memory. (Journal abstract modified)

228547 Lyubimov, B. I.; Boyko, S. S.; Mitrofanov, V. S.; Porfir'yeva, R. P.; Sharov, P. A. Laboratoriya obshchey farmakologii, Instituta farmakologii AMN SSSR, Moscow **/On the pharmacology of depot phthorphenazine./** K farmakologii ftorfenazina-depo. Farmakologiya i toksikologiya (Moskva). 38(4):393-397, 1975.

The pharmacological activity of depot phthorphenazine was compared with that of phthorphenazine dihydrochloride in both rats and mice. Depot phthorphenazine was found to have a prolonged action; a single injection was sufficient to depress conditioned avoidance reflexes for 45 to 50 days. The antagonism of the drug to amphetamine lasted for 30 days after its administration. Seventeen days after injection, phthorphenazine was found capable of prolonging the anesthetic action of sodium thiopental. The effects of single administration of depot phthorphenazine continued to be present in the blood and organ tissues for 4-5 weeks. Depot phthorphenazine was also found to be slightly toxic. 5 references. (Journal abstract modified)

228549 Popova, N. K. Laboratoriya populyatsionnoy farmakologii, Institute tsitologii i genetiki, Sibirskogo otdeleniya AN SSSR, Novosibirsk, U.S.S.R. **/The effect of imipramine on arousal from hibernation./** Vliyaniye imipramina na probuzhdeniye ot simney spyachki. Farmakologiya i toksikologiya (Moskva). 38(4):399-402, 1975.

The effect of imipramine on arousal from hibernation was investigated in gophers. Intraperitonal injections of imipramine (20-50mg/kg) delayed arousal from hibernation by 3-5 hours. Imipramine action differed from that of serotonin (5-HT) and 5-hydroxytryptophan (5-HTP) in that 5-HTP had a more pronounced effect on thermogenesis, thus inhibiting the warming up of the gophers, while imipramine affected the arousal action itself. Tranylcypromine failed to exert any substantial effect on either the warming up or arousal of gophers from hibernation. Tranylcypromine attenuated the action of imipramine. 9 references. (Journal abstract modified)

228630 Oppenheim, R. W.; Reitzel J. Neuroembryology Lab., Research Div., North Carolina Dept. of Human Resources, Box 7532, Raleigh, NC 27611 **Ontogeny of behavioral sensitivity to strychnine in the chick embryo: evidence for the early onset of CNS inhibition.** Brain, Behavior and Evolution (Basel). 11(2):130-159, 1975.

The development of behavioral sensitivity to strychnine was studied in the chick embryo between day 7 of incubation and 1 day posthatching. The earliest response to systemically applied strychnine was a marked depression of spontaneous motility at high concentrations of the drug. Lower concentrations had no effect at this time (6-7 days). About 2 days later, strychnine induced a statistically reliable, but brief, increase in spontaneous motility (hyperactivity). At 11 and 13 days, the brief excitatory response following strychnine had increased in duration to about 4 minutes. For the first time at 16 days myoclonic convulsions were observed following strychnine. At the same time the sensitivity of the embryo to strychnine increased compared to earlier stages. By 18 days, strychnine most often induced an immediate convulsive response without the preceding brief hyperactivity. This was also typical of newly hatched chicks. The systemic application of glycine at 9 and 13 days of incubation produced a slight, but statistically reliable, depression of ongoing spontaneous motility, consistent with what might be expected if glycine were acting as an inhibitory neurotransmitter. It typically took between 3 and 4 min following injection for this glycine response to occur. 96 references. (Author abstract modified)

229034 Huy, N. D.; Belleau, R.; Roy, P. E. Centre de recherche, Institute de Cardiologie de Quebec, 2725, chemin Ste-Foy, Sainte-Foy, Quebec, Canada E1V4E5 **Toxicity of marijuana and tobacco smoking in the beagle.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):267-276, 1975.

In a study chronic effects of marihuana, four cigarettes of marihuana or tobacco in the form of smoke inhaled into the trachea were administrated to dogs daily over a period of 9 months. Marihuana caused a slowing of bodyweight gain. Food consumption increased at first and was accompanied by diarrhea; then it decreased. This suggests a malabsorption of food or a more fundamental metabolic disturbance. The tobacco smoking group consumed much less food without showing any significant change in bodyweight gain until the ninth month. In marihuana smoking dogs, blood pressure remained unchanged. The resting heartrate was increased (by 32% at 3, 30% at 6, and 15% at 9 months). Alpha-globulin, eosinophils and lymphocyte count were significantly decreased. A decrease in serum triglycerides was noted. A behavior study indicated a general perturbation in the behavior of the marihuana smoking

dogs. Impairment of learning was shown, probably due to these behavioral perturbations. 25 references. (Author abstract modified)

229264 Shah, Nandkumar S.; Jacobs, J. R.; Jones, J. T.; Hedden, Martha P. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC **Interaction of mescaline with phenothiazines: effect on behavior, body temperature, and tissue levels of hallucinogen in mice.** Biological Psychiatry. 10(5):561-573, 1975.

In a study of the interaction of mescaline and phenothiazines, mescaline was injected in mice 45 min before chlorpromazine (CPZ), thioridazine, or chlorpromazine-sulfoxide (CPZ-SO). Excitement, agitation, slight increase in ventilation and occasional head shaking were seen 30 min after mescaline and continued for 30-45 min thereafter; locomotor activity and the number of scratching events were significantly increased during this period. CPZ and thioridazine partially or completely blocked mescaline induced gross behavior; CPZ-SO was not effective. Increased scratching responses and locomotor activity induced by mescaline were antagonized by all doses of CPZ and thioridazine; at higher doses, both CPZ and thioridazine induced a cataleptic like condition and marked hypothermia. Tissue levels of mescaline, examined 3 hr after its administration, were increased by all doses of CPZ and a higher dose of thioridazine; CPZ-SO and lower doses of thioridazine had no effect.

229286 Singh, Jasbir M. Alcoholism Services Unit, Department of Psychiatry, Charity Hospital of Louisiana, New Orleans, LA **Methadone-induced behavioral changes: circular movements, aggression, and electrophysiological aspects.** International Journal of the Addictions. 10(4):659-673, 1975.

Behavioral changes were induced in animals by methadone administration. The dose dependent CM effect was present 2-3 minutes after methadone administration. This effect can be partially blocked by nalline. A complete blockade occurred when the nalline reserpine combination was given prior to the administration of methadone. Atropine sulfate did not block the CM effect. Methadone withdrawal produced mild symptoms of aggression, and they were intensified by amphetamine and apomorphine. During the process of development of tolerance and addiction, electrophysiological changes were produced. These changes were intensified by apomorphine treatment in the methadone withdrawal animals. On the basis of pharmacological manipulation in experiment conditions, the involvement of cerebral biogenic amines, especially dopamine, is proposed. 23 references. (Author abstract)

229428 Kelleher, R. T. Harvard Medical School, New England Regional Primate Research Center, Southborough, MA **The importance of reinforcement schedules in determining effects of drugs.** Psychopharmacology Bulletin. 11(4):4-6, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974, the importance of reinforcement schedules in determining the effects of drugs was discussed, citing results from recent studies which show that the behavioral effects, as contrasted with the physiological effects, of drugs can be critically dependent upon the ways in which consequent events are scheduled. Findings from studies into the effects of amphetamine on reinforced responding in animals are particularly demonstrative of this requirement. The effects of amphetamine are largely independent of the type of event maintaining behavior, but critically dependent upon both dose and predrug rate of responding. This unified description of the behavioral effects of amphetamines has broad implications, including the observation that different schedule controlled levels of behavior in such an integrated system could alter the neurochemistry of the brain and, thus, modulate amphetamine's behavioral effects. 9 references. (Journal abstract modified)

229461 Cook, Leonard; Sepinwall, Jerry. Research Division, Hoffman-La Roche, Nutley, NJ **Behavior analysis of the effects and mechanisms of action of benzodiazepines.** Psychopharmacology Bulletin. 11(4):53-55, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, a study of the mechanism of action of the benzodiazepines in rats was reported, which tested the hypothesis correlating serotonin changes with the antianxiety activity of this drug. Two serotonin antagonists, methysergide and cinanserin, produced significant anticonflict effects. Methysergide and chlordiazepozide also had additive effects. Further experiments on the hypothesis were conducted in conflict trained drug naive rats, and results did not parallel previous ones. However, the hypothesis remains a useful one since the discrepancy may have been due to differences in the protocol. 12 references. (Journal abstract modified)

229475 Antelman, Seymour M. University of Pittsburgh, Pittsburgh, PA 15213 **The chemistry of reward and related behaviors.** Psychopharmacology Bulletin. 11(4):68-69, 1975.

The role of norepinephrine (NE) and dopamine (DA) in self-stimulation is being investigated in male rats to determine possible involvement of the catecholamines in the mediation of neural events and behaviors relating to hunger, thirst, and sex drives. Chronic depletion of whole brain catecholamine levels is attained by intraventricular injection of 6-hydroxydopamine (6-OHD), which is also applied to specific intracerebral sites to lesion selected catecholamine pathways. Pharmacological manipulations are carried out to selectively deplete NE or DA or to achieve a more massive depletion of both catecholamines following 6-OHDA treatment. Procedures are designed to assess the role played by receptor supersensitivity in abetting and/or later recovery of functions following catecholamine depletion. Acutely acting drugs are used in procedures to evaluate the contribution of each catecholamine to amphetamine induced facilitation of self-stimulation. Other studies will evaluate the effects of early, chronic depletion of catecholamines on self-stimulation and other drives during the developmental period and early adulthood. (Journal abstract modified)

229477 Buckley, Joseph P. University of Houston, Houston, TX 77004 **Evaluation of new compounds for psychotropic activity.** Psychopharmacology Bulletin. 11(4):69-70, 1975.

Compounds synthesized or extracted from plant materials by NIMH and NIH grantees are being evaluated for psychotropic activity to provide information about behavioral mechanisms of action and suggest possible uses for the drugs or to modify the structures of these agents for further study. Ss include mice, rats, dogs, and monkeys; pentobarbital, chlorpromazine (CPZ) and delta9-tetrahydrocannabinol (THC) are being studied. Results to date suggest that 7-hydroxy-CPZ may have potential use as a therapeutic agent. Five tricyclic aza analogs of THC produced a dose dependent depressant effect on spontaneous and forced motor activity. Crude extracts of H. tomentosa and H. pedunculata produced central nervous system depression, a decrease in spontaneous motor activity, and a potentiation of hexobarbital sleeping time. The H. tomentosa extract decreased rectal temperature and certain fractions induced ptosis. H. tomentosa was more pharmacologi-

cally active, possessing certain actions similar to cannabis. Data suggest that fraction C, and possibly fractions E and K, should be investigated in greater depth. (Journal abstract modified)

229479 Clark, Fogle C. University of Mississippi, University, MS 38677 **Drug-schedule interactions and intercurrent behavior.** Psychopharmacology Bulletin. 11(4):70-71, 1975.

The effects of drugs and reinforcement schedules on rewarded and intercurrent (competing, unreinforced) behavior were investigated to determine whether drugs with significant behavioral effects also characteristically influence the relations among different forms of schedule controlled and schedule induced behavior. Lever pressing to produce food is used with rats as the reinforced response, and both drinking and wheel running are recorded as intercurrent behaviors. Drugs include d-amphetamine, chlorpromazine, chlordiazepoxide, and atropine. Under fixed-interval schedules, the effects of the drugs on unreinforced behavior differed according to the particular pattern and sequential distribution of responses, but under space responding schedules, different patterns were observed in different Ss. Drug effects on lever pressing under direct schedule control were consistent among Ss within each procedure, but effects on nonreinforced responding depended upon Ss' baseline rate and sequential distribution of responses. Both level pressing and running rates increased and then decreased a function of amphetamine dose for all Ss under fixed-interval schedules, but only lever pressing rates showed such results under spaced responding schedules. (Journal abstract modified)

229484 Gebhart, Gerald F. University of Iowa, Iowa City, IA 52240 **Neuropharmacology of psychopharmacological agents.** Psychopharmacology Bulletin. 11(4):72-73, 1975.

The effect of various analgesic, tranquilizing and sedative agents on pain is being examined in cats, dogs, mice and other animals. Results indicate that administration of morphine, either alone or in conjunction with the delivery of painful stimuli, produces a significant increase in whole brain levels of gamma-hydroxybutyrate (GHB), a substance which may be related to the mechanism of action in narcotic analgesia. In other studies, pain raises the levels of both aspartate and glutamate in subcortical areas, while morphine decreased these levels. Preliminary data suggest that pain induced increases are related to the intensity of aversive stimuli. The biochemical and electrophysiological changes that may be associated with the analgesic state are currently being examined to refine the methodology. In drug studies, chlorpromazine was half as effective as morphine in easing pain in cats. In a separate study, it was demonstrated that the excitability of the limbic system was markedly altered by noxious stimuli. (Journal abstract modified)

229485 Green, Jack P. Mount Sinai School of Medicine, New York, NY **Drugs, behavior, and the cholinergic nervous system.** Psychopharmacology Bulletin. 11(4):73, 1975.

The role of cholinergic systems of the brain as neuroanatomic substrates for learning and memory and as sites of action for drugs that affect these processes is being examined, along with the pharmacological and functional relationships between the cholinergic nervous system and the dopaminergic, noradrenergic, and serotonergic systems of rats and mice. In initial studies, 20mg/kg doses of amphetamine caused an increase in acetylcholine levels in the corpus striatum which varied from animal to animal. In Ss showing greater increases in acetylcholine, there were comparatively small bilateral differences between the two striata in dopamine content, suggesting that striatal acetylcholine may modulate or inhibit the dopaminergic system. High affinity uptake of choline was rate limiting in the formation of acetylcholine, and this uptake was coupled to the process of acetylation. One of the compounds, N-hydroxyethyl-pyrrolidinium methiodide or pyrrolcholine,, appeared to be a precursor of a false transmitter, acetylpyrrolcholine, and impaired passive avoidance learning in a dose related manner. (Journal abstract modified)

229487 Leeming, Frank C. Memphis State University, Memphis, TN 38111 **Modification of the frustration effect with drugs.** Psychopharmacology Bulletin. 11(4):74-75, 1975.

The influences of various drugs on the frustration effect (FE) are being studied under a variety of conditions to identify drugs that act against the FE irrespective of the type of frustration experienced by male albino rats. In Skinner box studies, chlorpromazine (CPZ) produced omission test response rates which varied inversely with dose level. Response rates following reward also varied in this manner. Thus, CPZ appears to selectively reduce frustration, although it seems to depress behavior to some extent. In tests using activity to measure frustration, both 5mg/kg and 10mg/kg injection of Librium (chlordiazepoxide) increased the FE by about 20%. A .25mg/kg injection of reserpine also reduced the FE, while a .50mg/kg dose completely eliminated it. Because neither dose of reserpine affected activity level of control Ss, this drug appears to specifically reduce frustration. Runway goalbox studies with reserpine confirmed this finding, showing a dose related reduction of FE with no apparent effect on other behavior. (Journal abstract modified)

229488 Maengwyn-Davies, Gertrude D. Georgetown University, Washington, DC 20007 **Drugs, aggression, and neurochemistry.** Psychopharmacology Bulletin. 11(4):75, 1975.

Changes induced in the victim by his encounter with aggression are being studied to provide some insight into the potential pharmacological management of such victims. Experiments with aggressor mice, isolated for long periods to heighten tendency to attack and then exposed to victim mice, indicated the effects of aggression on the metabolic machinery of the catecholamines of brain and blood, as well as those in the adrenal medulla. Measurements are made of tyrosine hydroxylase, phenylethanolamine-N-methyltransferase, dopamine, norepinephrine, and epinephrine in the tissues. The time course of the effect is followed, as well as that of the disappearance of the aggression induced changes following cessation of attacks. The actions of various classes of psychoactive drugs on biochemical changes induced by aggression are assessed by giving the drugs before the attacks to determine their protective effects or after the attacks to identify which ones alter the rate of recovery. The research is presently in the data collection stage. (Journal abstract modified)

229499 Zigmond, Michael J. University of Pittsburgh, Pittsburgh, PA 15213 **Neuropharmacology of brain monoamines and behavior.** Psychopharmacology Bulletin. 11(4):80, 1975.

The role of prominent catecholamine brain projections in various types of motivated behavior is being examined in male rats. Neurophysiological studies of normal and brain damaged Ss are expected to generate data relevant to problems of mental health and cerebral dysfunction, including Parkinson's disease and mental retardation. Results to date indicate that brain catecholamine biosynthesis is inhibited by elevations in amine concentration, but transamination of tyrosine is unaffected. Injection of 6-hydroxydopamine (6-HDA) produces an initial

decrease in fixed ratio response rate, but performance returned to normal within 4 days. The data suggest that adaptations within catecholamine containing systems were responsible for this recovery. Food and water intake and sexual behavior were also impaired by disruptions of catecholamine containing brain systems, and these effects may have been due mainly to nonspecific motivational deficits. (Journal abstract modified)

229639 Smith, James B.; Clark, Fogle, C. Worcester Foundation for Experimental Biology, 222 Maple Ave., Shrewsbury, MA 01545 **Effects of d-amphetamine, chlorpromazine, and chlordiazepoxide on intercurrent behavior during spaced-responding schedules.** Journal of the Experimental Analysis of Behavior. 24(2):241-248, 1975.

The effects of d-amphetamine (A), chlorpromazine (CPZ), and chlordiazepoxide (CDZ) on lever pressing under direct control of spaced responding schedules were compared with their effects on intercurrent drinking and wheel running in the rat. Drug effects on lever pressing were systematically related to dose and were consistent for all animals; drug effects on intercurrent behavior were generally different for each animal. In the case of lever presses, increasing doses of A first increased and then decreased response rate, increasing doses of CPZ produced graded decreases in response rate, and doses of CDZ up to 40mg/kg produced no effect on response rate. The results are discussed in terms of the concept of schedule controls, and it is suggested that the behavioral pharmacology of intercurrent behavior be explored as a procedure in the experimental analysis of intercurrent behavior. 30 references. (Author abstract modified)

229680 Pisarski, Wlodzimierz. Oddzial Neurologiczny Osrodka Naukowego AM, ZOZ Praga-Poludnie, Szaserow 2, 04-293 Warsaw, Poland **/Effect of 5,5-diphenylhydantoin (DPH) on learning and memory in cats./** Wplyw 5,5'-dwufenylohydantoiny (DPH) na uczenie i pamiec u kotow. Neurologia i Neurochirurgia Polska (Warszawa). 8(3):437-440, 1974.

An experiment was conducted to evaluate the effect of prolonged administration of diphenylhydantoin (DPH) in doses of 15-20mg/kg on learning and memory in eight adult cats. The findings show prolongation of learning and slight prolongation of development of the conditioned reflex, and significant prolongation of the development of the differential inhibitory reflex. Normal memory of the conditioned reflex and disturbed memory of the differential inhibitory reflex were found. A correlation was observed between the serum DPH level, toxic manifestations of the drug, and the learning time. No correlation was seen between drug dosage and its serum level. 4 references. (Journal abstract)

229681 Iwinska, Bozena. Instytut Psychoneurologiczny, Sobieskiego 1/91, 02-957 Warsaw, Poland **/Effect of 5,5'-diphenylhydantoin on fixed conditioned reflexes in cats./** Wplyw 5,5'-dwufenylohydantoiny na utrwalone odruchy warunkowe kotow. Neurologia i Neurochirurgia Polska (Warszawa). 8(3):441-447, 1974.

The effect of 5,5'-diphenylhydantoin administered in nontoxic doses on conditioned reflexes developed and fixed in cats prior to drug administration is reported. The investigations were carried out with two groups of four cats receiving the drug and a control group. The drug was given usually in a dose of 7.5mg/kg of bodyweight during a period of 6-8 weeks. The drug disturbed the reflexes in all animals and induced changes in unconditioned behavior of animals and in their general condition independent of the drug dosage 3 and 4 weeks after the initiation of drug therapy. 14 references. (Journal abstract)

230007 Gut, I.; Becker, B. A. Institute of Hygiene and Epidemiology, Center of Industrial Hygiene and Occupational Diseases, Prague, Czechoslovakia **Heredity of hexobarbital sleeping time and efficiency of drug metabolism in Wistar and Sprague-Dawley rats.** Archiv fur Toxikologie (Berlin). 34(1):61-70, 1975.

The nature of considerable variability of hexobarbital sleeping time and drug metabolism efficiency within a single strain of rats was investigated. Wistar or Sprague-Dawley Ss with shorter than average hexobarbital sleeping time also had higher rates of in vitro hepatic microsomal metabolism of hexobarbital, aminopyrine, aniline and benzene. They also had higher liver weight, microsomal protein content and P-450 level and faster hexobarbital blood level decline after intraperitoneal hexobarbital sodium than those with relatively longer hexobarbital sleeping time, but awakened with the same blood level. Differences were maintained throughout the life of Ss and inherited in their offspring, suggesting a possible genetic control of hexobarbital sleeping time and efficiency of drug metabolisms with apparent differences in selection response to type one and type two substrates (hexobarbital and aminopyrine vs. aniline). Different heredity mechanism for these types of substrates may exist. 15 references. (Author abstract modified)

230452 Wauquier, A.; Niemegeers, C. J. E. Dept. of Pharmacology, Janssen Pharmaceutica Research Labortoria, B-2340 Beerse, Belgium **The effects of dexetimide on pimozide-, and haloperidol- and pipamperone-induced inhibition of brain self-stimulation in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 217(2):280-292, 1975.

The effects of 0.63mg/kg of dexetimide on the inhibition of brain self-stimulation in rats produced by four subcutaneous doses of pimozide, haloperidol and pipamperone was examined. The lowest dose of each neuroleptic did not affect self-stimulation; the second dose inhibited the response rate by approximately 50%, and the two highest doses completely suppressed self-stimulation behavior. Dexetimide administered subcutaneously completly antagonized the pimozide induced inhibition; the haloperidol induced inhibition was also completely antagonized except at its highest dose, whereas the effects of pipamperone were not antagonized. Data are consistent with a presumed dopaminergic/cholinergic striatal interaction and show brain self-stimulation to be an effective measure of neuroleptic anticholinergic interaction. 25 references. (Author abstract modified)

230570 Izquierdo, Ivan. Departmento de Fisiologia, Escola Paulista de Medicina, Rua Botucatu 862, 04023 Sao Paulo, SP, Brazil **Relations between orienting, pseudoconditioned and conditioned responses in the shuttle-box -- a pharmacological analysis by means of LSD and dibenamine.** Behavioral Biology. 15(2):193-205, 1975.

The effect of lysergic acid diethylamide (LSD) (0.075mg/kg and 0.3mg/kg) on orienting and on shuttle responses to a buzzer was investigated in rats submitted to three different experimental procedures in a shuttlebox: 1) habituation, 2) pseudoconditioning, and 3) two-way avoidance. LSD increased orienting response in all three situations in a dose dependent fashion, and dibenamine (10mg/kg), had a similar action. LSD also enhanced performance of pseudoconditioned responses in a dose dependent fashion, an effect potentiated by dibenamine. In the two-way situation, pretrial LSD increased shuttle responses only at the lower dose, and when given together with dibenamine it was depressant at both doses. Retention was lower in all LSD groups than in water or dibenamine treated groups. It is concluded that LSD has a

deleterious effect on acquisition of the shuttle response. Dibenamine alone had no effect on either conditioned or pseudoconditioned shuttling. These results indicate that orienting, pseudoconditioned shuttling and conditioned shuttling each have a distinct pharmacology of their own. 21 references. (Author abstract modified)

230577 Eisenstein, Norman; D'Amato, Michael R. Schering Corporation, Department of Pharmacology, 60 Orange St., Bloomfield, NJ 07003 **Effects of magnesium pemoline on a delayed match-to-sample task in monkeys.** Behavioral Biology. 15(2):245-250, 1975.

The effects of magnesium pemoline on retention were examined in monkeys (Cebus apella) previously trained in a delayed match to sample paradigm, in order to distinguish between drug effects on learning and retention. Three monkeys were dosed orally at 0.25mg/kg, 1mg/kg, 2mg/kg, 4mg/kg, and 16mg/kg with magnesium pemoline and tested at three fixed delays (2 sec, 60 sec, and 180 or 300 sec). There was no effect on retention of the sample although the data suggest that magnesium pemoline interferes with previously stable retention of the sample at the short delay (2 sec). 28 references. (Author abstract)

230825 Davis, W. Marvin; Smith, Thomas P. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Morphine enhancement of shuttle avoidance prevented by alpha-methytyrosine.** Psychopharmacologia (Berlin). 44(1):95-97, 1975.

The inhibition of morphine enhancement of shuttle avoidance in rats by alpha-methyl-tyrosine (amt) is reported. Both morphine sulfate and d-amphetamine sulfate increased the avoidance level by 70-100%. Prior treatment with amt prevented the effects of both drugs. Nalorphine hydrochloride also blocked the effect of morphine. The action of amt to block enhancement of avoidance is taken to indicate that this effect of morphine is attributable to a catecholamine dependent excitatory component of its activity profile. 14 references. (Author abstract modified)

230828 Einon, Dorothy; Tye, N. C. Psychological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EB, England **Chlordiazepoxide and isolation induced timidity in rats.** Psychopharmacologia (Berlin). 44(1):83-85, 1975.

The effects of chlordiazepoxide (CDP) on emergence behavior was examined in socially reared and isolation reared rats. It was found that low doses of CDP decreased the emergence times of isolated animals but had little effect on the emergence of social animals. At higher doses the drug retarded emergence in all groups but there were no differential effects. The results do not support claims that rearing conditions influence the susceptability of rats to CNS depressants, rather they suggest that particular levels of CDP selectively influence emotional behavior. 13 references. (Author abstract)

230829 Goudie, A. J.; Thornton, E. W. Department of Psychology, University of Liverpool, Eleanor Rathbone Building, P.O. Box 147, Liverpool L69 3BX, England **Effects of drug experience on drug induced conditioned taste aversions: studies with amphetamine and fenfluramine.** Psychopharmacologia (Berlin). 44(1):77-82, 1975.

The effects of drug experience on drug induced conditioned taste aversions (CTAs) were examined in rats. CTAs established in rats to 0.1% sodium saccharin by intraperitoneal injections of DL-fenfluramine hydrochloride or d-amphetamine sulphate were found to be significantly attenuated, but not abolished altogether, by chronic pretreatment with the specific drug. Prior treatment with fenfluramine attenuated the aversive effects of amphetamine, but the converse was found not to be the case. These results are considered to refute the unnatural need state and novelty hypotheses of the effects of prior drug experience on the establishment of CTAs. An alternative explanation of such effects in terms of tolerance is considered, and the possible relevance of the results to studies of drug abuse in humans discussed. 25 references. (Author abstract)

230831 Huppert, Felicia A.; Iversen, Susan D. Department of Experimental Psychology, Downing Street, Cambridge, England **Response supression in rats: a comparison of response-contingent and noncontingent punishment and the effect of the minor tranquillizer, chlordiazepoxide.** Psychopharmacologia (Berlin). 44(1):67-75, 1975.

A comparison of the behavioral effects of response contingent and noncontingent shock was carried out in a series of experiments examining suppression of an operant response (bar-pressing) release from suppression following injection of the minor tranquilizer chlordiazepoxide, and suppression of behavior in a situation not associated with shock. Response contingent shock produced far greater suppression of the operant response than did noncontingent shock, as well as greater suppression of behavior in a neutral environment following the shock experience. Chlordiazepoxide was found to be far more effective in relasing behavior from suppression when shock was response contingent than when shock was noncontingent, a result which does not appear to reflect simply the greater suppression produced by response contingent shock. 14 references. (Author abstract modified)

230836 Colasanti, Brenda K.; Kosa, Jane E.; Craig, Charles R. Department of Pharmacology, West Virginia University Medical Center, Morgantown, VA 26506 **Appearance of wet dog shake behavior during cobalt experimental epilesy in the rat and its supression by reserpine.** Psychopharmacologia (Berlin). 44(1):33-36, 1975.

The incidence of wet dog shakes in cobalt epileptic rats and in rats bearing similar cortical lesions produced by glass rods was explored. The effect of reserpine on the appearance of wet dog shakes in both naive and cobalt epileptic rats was also examined. The number of wet dog shakes exhibited by the control rats remained at a low and constant level over 18 days of recording. In contrast, wet dog shakes in the chronically epileptic rats began to increase by the fourth day after cobalt placement and remained significantly elevated up to the 18th day. Administration of reserpine to naive rats or to cobalt epileptic rats on days 7 and 9 after implantation resulted in an almost complete suppression of wet dog shakes which endured over a period of 3-5 days. These results suggest that the abnormally elevated wet dog shake response of the cobalt epileptic rats and the spontaneous wet dog shake behavior of normal rats may be mediated by common neural pathways. 14 references. (Author abstract modified)

230837 Winter, J. C. 122 Capen Hall, SUNY, Buffalo, NY 14214 **The effects of 2,5-dimethoxy-4-methylamphetamine (DOM), 2,5-dimethoxy-4-ethylamphetamine (DOET), d-amphetamine, and cocaine in rats trained with mescaline as a discriminative stimulus.** Psychopharmacologia (Berlin). 44(1):29-32, 1975.

The effects of 2,5-dimethoxy-4-methylamphetamine (DOM), 2,5-dimethoxy-4-ethylamphetamine (DOET), d-amphetamine,

and cocaine were examined in rats trained with mescaline as a discriminative stimulus. Administration of a range of doses of DOM and DOET to subjects in which saline functioned as discriminative stimulus (SD) and mescaline as S delta revealed that a dose of 0.3mg of either DOM or DOET was equivalent to the training dose of mescaline. When tested in rats in which mescaline served as SD, DOM and DOET were likewise found to mimic mescaline. In contrast, doses of d-amphetamine and cocaine which were equivalent to the training dose of mescaline as S delta did not result in responding appropriate for the mescaline condition when mescaline was trained as SD. When DOET was substituted for saline as S delta, no evidence of discriminated responding was obtained in the course of 50 sessions. The data suggest that those effects of mescaline in the rat which function as a discriminative stimulus are better correlated with prehallucinogenic LSD like activity in man then with hallucinogenic activity per se. These effects in rats represent a necessary but not a sufficient condition for prediction of hallucinogenic activity in man. 24 references. (Author abstract modified)

230838 Leaf, Russell, C.; Wnek, D.J.; Gay, Patricia E.; Corcia, R. M.; Lamon, Stacy. Rutgers College, Rutgers University, New Brunswick, NJ 08903 **Chlordiazepoxide and diazepam induced mouse killing by rats.** Psychopharmacologia (Berlin). 44(1):23-28, 1975.

The hypothesis that the effects of the malaise produced by pilocarpine could also be blocked by the tranquilizing effects of chlordiazepoxide was tested in relation to mouse killing by rats. Chlordiazepoxide HCl significantly increased the low base rates of mouse killing (3-9%) observed in large samples of Holtzman strain albino male rats. Diazepam was equally effective, and several times more potent than chlordiazepoxide. Pentobarbital did not increase killing. Killing induced by chlordiazepoxide was blocked by d-amphetamine sulfate but not by l-amphetamine, at dose levels similar to those that block undrugged killing in this strain. Unlike pilocarpine induced killing, the effects of chlordiazepoxide were not increased or decreased significantly by either peripherally or centrally active anticholinergic drugs, over wide dose ranges of these agents; nor were the effects of chlordiazepoxide increased by repeated daily administration. 25 references. (Author abstract modified)

230842 MacPhail, Robert C.; Seiden, Lewis S. Department of Pharmacological and Physiological Sciences, University of Chicago, 947 East 58th St., Chicago, IL 60637 **Time course for the effects of cocaine on fixed-ratio water-reinforced responding in rats.** Psychopharmacologia (Berlin). 44(1):1-4, 1975.

The effect of dose and pretreatment time of cocaine on the lever pressing of rats maintained by a fixed-ratio schedule of water delivery was examined. When given 15 min prior to a session, cocaine in all rats produced dose related decreases in responding. The largest dose, when given 15 min presession to two rats, almost completely suppressed responding. Lengthening the time between drug injection and test session attenuated the rate decreasing effects of cocaine. Cocaine effects depend on the dose as well as the time of its administration prior to testing. 21 references. (Author abstract modified)

230864 Golub, Mari; Kornetsky, Conan. 2713 Green Bay Way, Sacramento, CA 95826 **Modification of the behavioral response to drugs in rats exposed prenatally to chlorpromazine.** Psychopharmacologia (Berlin). 43(3):289-291, 1975.

Female rats exposed prenatally to low levels of chlorpromazine were examined and compared to males. Females were less susceptible as adults to the rate reducing effects of chlorpromazine and pentobarbital on fixed-interval performance of a food reinforced operant. Males were not significantly affected by prenatal treatment. 12 references. (Author abstract)

230865 Avis, Harry H.; Peeke, Harman V. S. Laboratory of Psychobiology, University of California, Langley Porter Institute, San Francisco, CA 94143 **Differentiation by morphine of two types of aggressive behavior in the convict cichlid (Cichlasoma nigrofasciatum).** Psychopharmacologia (Berlin). 43(3):287-288, 1975.

Differentiation by morphine of two types of aggressive behavior was examined in the convict cichlid (Cichlasoma nigrofasciatum). Morphine sulfate significantly decreased the amount of territorial aggression in the convict cichlid. The same doses had no effect on predatory aggression (ingestion of brine shrimp). The data suggest that the previously demonstrated morphine receptor in the fish has functional properties. 7 references. (Author abstract)

230868 Grilly, David M. Department of Psychology, Cleveland State University, Cleveland, OH 44115 **Effects of prior experience on differential learning under amphetamine.** Psychopharmacologia (Berlin). 43(3):271-277, 1975.

Differential learning of operant behavior under nondrug and amphetamine states was examined in rats with a drug behavior reinforcement interaction process. It was hypothesized that when a drug affects the relationship between ongoing behavior and existing reinforcement contingencies, the sets of behavioral patterns subjected to the process of reinforcement or nonreinforcement under a drug may differ from the patterns under nondrug conditions. Results indicate that amphetamine significantly enhanced performance, and this enhancement transferred to subsequent nondrug conditions. If nondrug training occurred before drug training, this enhancement was greatly attenuated. Only those behavioral components under which amphetamine led to an increase in reinforcement rate showed enhancement in the nondrug state. The results, which supported the present position, were discussed in relation to a stimulus generalization decrement explanation of differential learning under amphetamine. 24 references. (Author abstract modified)

230869 Kjellberg, B.; Randrup, A. AB Ferrosan, Pharmacological Department, Malmo, Sweden **Behavioural effects of thymoleptics in vervet monkeys (Cercopithecus aethiops).** Psychopharmacologia (Berlin). 43(3):267-269, 1975.

The behavioral effects of thymoleptics were examined in vervet monkeys (Cercopithecus aethiops). It was found that desmethylimipramine (DMI) exerts diverse quantitative effects on the gross behavior of monkeys. Excitatory as well as sedative effects were observed, which varied according to the general animal temperament. Results resembling those obtained with DMI were observed using chlorimipramine and iprindole, although the effects of iprindole were less marked. Chlorimipramine also produced immobilization and postural change. The results are discussed in relation to behavioral effects of thymoleptics in humans, and the use of monkeys in preclinical testing of thymoleptic drugs is suggested. 12 references. (Author abstract)

230870 Lush, I. E. Royal Free Hospital School of Medicine, 8 Hunter St., London WC1N 1BP, England **A relationship between hexobarbitone sleeping time and susceptibility to mescaline in mice from different strains.** Psychopharmacologia (Berlin). 43(3):259-260, 1975.

Males from the following strains of mice were surveyed with respect to their hexobarbitone sleeping time: A2G, C57BR, C3H, F/st, CBA, ICFW and Schneider. Males from the same strains had previously been surveyed with respect to the inhibitory effect of mescaline on their emotional defecation. There is a strong interstrain correlation between the two measures. This correlation was unexpected on theoretical grounds and may have important pharmacogenetic implications. 6 references. (Author abstract)

230872 Rezek, Milan; Novin, Donald. Department of Physiology, University of Manitoba, Winnipeg, Manitoba, Canada **The effects of serotonin on feeding in the rabbit.** Psychopharmacologia (Berlin). 43(3):255-258, 1975.

The effects of serotonin on feeding were examined in the rabbit. Serotonin infused through hepatic portal cannulae of rabbits decreased food intake in a free feeding condition. Following a 12 hr food deprivation period similar doses of serotonin increased food intake. Results demonstrate that serotonin is not a simple satiety hormone but may be importantly involved in short-term regulatory mechanisms of feeding. 17 references. (Author abstract modified)

230874 Tessel, Richard E.; Woods, James H. Department of Pharmacology, University of Colorado Medical School, Denver, CO 80220 **Fenfluramine and N-ethyl amphetamine: comparison of the reinforcing and rate-decreasing actions in the rhesus monkey.** Psychopharmacologia (Berlin). 43(3):239-244, 1975.

N-ethyl amphetamine HCl (NEA) and fenfluramine HCl (meta-trifluoromethyl N-ethyl amphetamine) were evaluated as reinforcers in rhesus monkeys that had been previously trained to press a lever using food presentations and cocaine HCl injections as reinforcers. Compared to saline, none of the drugs altered the rate of responding in the food periods which preceded the drug sessions, indicating the absence of residual response disrupting drug actions from previous sessions. NEA and fenfluramine self-injection resulted in dose related decreases in response rates during the food periods which immediately followed the drug sessions. Cocaine HCl maintained high response rates at over one response/second during the drug periods, as did the same dose of NEA. Doses of NEA as well as doses of fenfluramine HCl maintained rates that were not different from those associated with saline injections. The results indicate that fenfluramine's failure to act as a reinforcer is attributable to its meta-trifluoromethyl group. 19 references. (Author abstract modified)

230875 Drewnowski, Adam; Gray, Jeffrey A. Rockefeller University, New York, NY 10021 **Influence of delta9-tetrahydrocannabinol on partial reinforcement effects.** Psychopharmacologia (Berlin). 43(3):233-237, 1975.

The effects of delta9-tetrahydrocannabinol (THC) on partial reinforcement were examined in rats. Two experiments were performed with rats trained with either continuous reinforcement (food) or random 50% partial reinforcement for running in a straight alley. Half the rats were trained with daily injections of 0.5mg/kg THC and half with vehicle injections, all animals being extinguished with vehicle injections in experiment 1 and with THC injections in experiment 2. The partial reinforcement acquisition effect was abolished by THC during training; the partial reinforcement extinction effect was abolished by THC either during training or during extinction. In these respects THC resembles amylobarbitone and alcohol. 16 references. (Author abstract)

230876 Greenberg, I.; Kuhn, D. M.; Appel, J. B. Drug Research Unit, McLean Hospital, Belmont, MA Behaviorally **induced sensitivity to the discriminable properties of LSD.** Psychopharmacologia (Berlin). 43(3):229-232, 1975.

Behaviorally induced sensitivity to the discriminable properties of lysergic acid diethylamide (LSD) in rats is reported. Choice responding during extinction periods (no water reinforcement for either response) indicated a high level of discriminability (95% correct) following either LSD or saline. A dose response curve for LSD, obtained by tests for level choice after injections of 10, 20, 30, 40, 50, and 60 micrograms/kg, indicated that 10 micrograms/kg produced only 30% responding on the LSD level. This percentage was increased (to 83%) by reinforcing responding on the LSD level following injections of 10 micrograms/kg. Subsequent tests indicated that doses of 5.0and 2.5micrograms/kg produced a majority of responses on the LSD level. Since at these low doses LSD has few measurable biochemical or behavioral effects, it is hypothesized that the discriminable cue of LSD is related to direct stimulation of central serotonergic receptors. 24 references. (Author abstract modified)

230878 Hine, Bromfield; Wallach, Marshall B.; Gershon, Samuel. Department of Psychiatry, New York University School of Medicine, New York, NY 10016 **Involvement of biogenic amines in drug-induced aggressive pecking in chicks.** Psychopharmacologia (Berlin). 43(3):215-221, 1975.

In a study of drug induced aggression, different biogenic amines involved in aggressive pecking induced by an antidepressant (imipramine) and a general central nervous system stimulant (d-amphetamine) were examined. Although pecking was induced by tricyclics, d-amphetamine, and L-dopa, both pargyline, a monamine oxidase inhibitor, and imprindole, a tricyclic antidepressant, were ineffective. In a second experiment, pairs of chicks were pretreated with various doses of amine antagonists, and a standard dose of imipramine (IMI) or d-amphetamine (AMP) was administered. Haloperidol completely antagonized AMP but not IMI pecking, while phentolamine and propranolol did not modify AMP pecking, suggesting involvement of dopamine. Pecking induced by IMI was partially antagonized by a dose of methysergide ineffective in modifying AMP pecking. Neither phentolamine nor propranolol blocked IMI pecking. Serotonin was further implicated in IMI pecking in a third experiment where chronic p-chlorophenylalanine (PCPA) pretreatment significantly decreased IMI, but not AMP pecking. These data suggest that aggressive pecking induced by AMP and IMI may be mediated by different amine systems. 20 references. (Author abstract modified)

230879 Risner, Marc E.; Jones, B. E. NIDA Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **Self-administration of CNS stimulants by dog.** Psychopharmacologia (Berlin). 43(3):207-213, 1975.

In a study of self-administration of central nervous system stimulants, drug naive dogs were trained to respond for intravenous infusions of either d-amphetamine, phenmetrazine, or methylphenidate until a stable response rate per 4 hr daily session was achieved. An inverse relationship between unit dose and number of self-administered infusions per session was seen. Thus, total drug intake per session remained relatively constant and was independent of unit dose. Using a parallel line bioassay design, the relative potencies of d-amphetamine, phenmetrazine, and methylphenidate to maintain self-administration were estimated. By comparing the unit doses of d-amphetamine which yielded the same rate of self-

administration it was found that 1mg of phenmetrazine is equivalent to 0.1mg of d-amphetamine. It was also determined that 1mg of methylphenidate is equivalent to 0.75mg of d-amphetamine. These data indicate the dog can be used to assess the reinforcing properties of psychomotor stimulants. 30 references. (Author abstract modified)

230880 Colasanti, Brenda; Khazan, Naim. Department of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Electroencephalographic studies on the development of tolerance and cross tolerance to mescaline in the rat.** Psychopharmacologia (Berlin). 43(3):201-205, 1975.

The effect of chronic administration of mescaline on the electroencephalogram (EEG) and sleep/wakefulness cycle were examined in the rat. Recordings of the EEG and the electromyogram (EMG) were collected continuously from rats equipped with permanent cortical and temporalis muscle electrodes. The initial injections of the mescaline induced an immediate desynchronization of the EEG and behavioral arousal of the rat, which endured for 2-3 hrs. After this time, slow wave (SW) sleep and rapid eye movement (REM) sleep episodes reappeared, with the return of regular alternations of the sleep/wakefulness cycle. Upon continued administration of the drug, partial tolerance to the arousal effects of mescaline developed, which was reflected by a gradual reduction in the latencies to onset of SW sleep and REM sleep. Rats rendered tolerant to mescaline in this manner were found to be cross-tolerant to lysergic acid diethylamide (LSD) and N,N-diethyltryptamine (DET). In contrast, cross-tolerance did not occur to amphetamine, which exerts similar arousal and EEG desynchronizing effects. These results agree with physiological and behavioral studies of tolerance and cross-tolerance among hallucinogens and support the usefulness of the EEG as a quantitative indicator of central nervous system functions. 24 references. (Author abstract modified)

231005 Evans, Hugh L. Department of Radiation Biology, University of Rochester School of Medicine, Rochester, NY 14642 **Scopolamine effects on visual discrimination: modifications related to stimulus control.** Journal of Pharmacology and Experimental Therapeutics. 195(1):105-113, 1975.

In a study of the effects of scopolamine on visual discrimination stumptail monkeys (Macaca arctoides) performed a discrete trial, three choice visual discrimination. Strength of the stimuli in controlling behavior was systematically related to a physical property of the stimuli, luminance. Low luminance provided weak control, resulting in a low accuracy of discrimination, a low response probability and maximal sensitivity to scopolamine. High luminance provided strong control of behavior and attenuated the effects of scopolamine. Scopolamine effects resembled the effects of reducing stimulus control in undrugged monkeys. Since behavior under weak control seems to be especially sensitive to drugs, manipulations of stimulus control may be particularly useful whenever determination of the minimally effective dose is important, as in behavioral toxicology. Results are interpreted as specific visual effects of the drug, since nonsensory factors such as base line response rate, reinforcement schedule, training history, motor performance and motivation were controlled. Implications for state dependent effects of drugs are discussed. 38 references. (Author abstract modified)

231069 Salimov, R. M. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy otdela farmakologii, Instituta farmakologii, AMN SSSR, Moscow, U.S.S.R. **/The effect of psychotropic drugs on conditioned reflexes after an emotional stress in cats./** Vliyaniye psikhotropnykh veshchestv na uslovnyye refleksy u koshek posle emotsional'nogo vozbuzhdeniya. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 80(8):61-63, 1975.

The effect of psychotropic drugs on conditioned reflexes was investigated in 19 cats following experimentally induced rage and fear. Emotional stress destroyed differential inhibition and short-term memory in cats. Stelazine, haloperidol, amitriptyline, imizine, chlordiazepoxide, diazepam and benactyzine prevented these disturbances. Chlorpromazine, stelazine and haloperidol in high doses, however, enhanced the disturbances. Tranquilizers and antidepressants normalized higher nervous activity when administered in greater doses than the neuroleptics, and were more effective in the elimination of the negative consequences of strong emotional reactions. 14 references. (Journal abstract modified)

231119 Grigor'yeva, O. N. Kafedra farmakologii, Leningradskogo pediatricheskogo meditsinskogo instituta, Leningrad, U.S.S.R. **/Changes in excitability of the hippocampus after stimulation of serotonergic systems in rabbits of different ages./** Izmeneniye vozbudimosti gippokampa krolikov raznogo vozrasta pod vliyaniyem stimulyatsii serotoninergicheskikh sistem. Fiziologicheskiy zhurnal SSSR imeni I. M. Sechenova (Leningrad). 61(9):1318-1322, 1975.

The role of the serotonergic systems in the excitability of the hippocampus was investigated in 6-10-day-old, 16-20-day-old, and adult rabbits. Chemical electrodes were implanted in the left and right dorsal hippocampus. 5-Methoxytryptamine (mexamine) decreased the amount of seizures in the hippocampal penicillin epileptogenic focus in the 6-10 and 16-20-day-old rabbits, but had no effect on interictal epileptiform discharges in the electroencephalogram (EEG). Intravenous injections of mexamine inhibited seizures and interictal epileptiform EEG activity in 16-20-day-old rabbits, but had no effect on hippocampus epileptogenic foci in adult rabbits. It is concluded that the level of serotonergic systems activity more significantly affects hippocampus excitability in young rabbits than in adult ones. 27 references. (Journal abstract modified)

231248 Arushanyan, E. B.; Karpov, V. N. Kafedra farmakologii Meditsinskogo instituta, Chita, USSR **/The influence of d,l-amphetamine and caffeine on caudate inhibition of conditioned avoidance reactions in cats./** Vliyaniye fenamini kofeina na kaudatnoye tormozheniye uslovnoreflektornoy reaktsii izbeganiya u koshek. Zhurnal vysshey nervnoy deyatel'nosti imeni I.P. Pavlova (Moskva). 25(4):744-751, 1975.

The effect of phenamine (d,l-amphetamine) and caffeine on caudate inhibition of conditioned avoidance reactions was investigated in 13 cats preliminarily conditioned to avoid electrical shock. Stimulation of the caudate nucleus was found to inhibit behavioral response by lengthening its latency and reducing the number of conditioned reactions. The intensity of the inhibitory effect did not significantly depend on the localization of electrodes in the head or the body of the nucleus. Both phenamine and caffeine were found to suppress the caudate inhibition, but the action of the drugs was manifested in different ways. The influence of larger doses of phenamine (4 milligrams per kilogram) was characterized by a serious disturbances of behavior and by caudate inhibition of conditioned responses. The caudate inhibition suppressive action of caffeine was more direct than that of phenamine. 19 references. (Journal abstract modified)

231251 Komissarov, I. V.; Krivobok, G. K.; Talalaenko, A. N. Kafedra farmakologii Donetskogo meditsinskogo instituta

im. A. M. Gor'kogo, Donetsk, USSR /**Monoaminergic influences of the caudate nucleus on conditioned food-procuring reactions in rats.**/ Monoaminergicheskiye vliyaniya khvostatogo yadra na uslovnuyu pishchedobyvatel'nuyu reaktsiyu u krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I.P. Palvova (Moskva). 25(4):769-777, 1975.

The effect of microinjections of monoamines and glutamic acid into the caudate nucleus on conditioned alimentary procuring reactions was investigated in 21 rats. Dopamine, noradrenaline and glutamic acid were found to prolong the latency of the reflex, while serotonin reduced its latency. All the drugs tested, however, reduced the number of conditioned food procuring movements. The effects of dopamine were achieved through neuron receptors of the caudate nucleus which were sensitive to haloperidol and chlorpromazine; the effects of serotonin were mediated through the systems; those of noradrenaline were mediated through the alpha-adrenoreactive systems of the neostriatal neurons. The inhibitory effect of glutamic acid was not due to the action of the serotonergic, adrenergic, or dopaminergic receptors of the caudate units. 30 references. (Journal abstract modified)

231301 Fleisher, Lloyd N.; Glick, Stanley D. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, New York, NY 10029 **A telencephalic lesion site for D-amphetamine-induced contralateral rotation in rats.** Brain Research (Amsterdam). 96(2):413-417, 1975.

A telencephalic lesion site for D-amphetamine induced contralateral rotation is reported in rats. Two claustrum rats that were tested with apomorphine hydrochloride rotated opposite to the D-amphetamine direction. This might result from desensitization of the dopamine receptors in the striatum on the same side as the claustrum lesion by a nigrostriatal pathway firing at supranormal rates. Lesions of the ventrolateral caudate putamen produced the usual D-amphetamine induced ipsilateral rotation observed with more medial lesions. The results of the lesions suggest that combined caudate claustrum lesions tend to cancel each other so that rotational preference is not significantly changed. Lesions of the tuberculum olfactorium had no effect on rotational preference. 18 references.

231316 Shibuya, T.; Matsuda, H.; Endo, T.; Chen, P. O.; Sato, K.; Nishimori, T. Department of Pharmacology, Tokyo Medical College, Tokyo, Japan **Pharmacological studies of drug action on CNS, with special reference to effects of maprotiline.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(3):192-204, 1975.

The effects of maprotiline, mainly on the central nervous system, were examined and compared with those of imipramine, methamphetamine and chlorpromazine. In the repeated administration and the stroboscope studies, maprotiline exhibited actions to increase behavioral activities of animals, just like amphetamine, and imipramine. This appears to attest to pharmacological effects of maprotiline as an antidepressant. It is noted, however, that whereas maprotiline shows a slight antiapomorphine action in dogs and an inhibition of the spinal reflex action potential in cats, such actions are not recognized in other antidepressants of the tricyclic group including imipramine, amitriptyline, etc. These differences suggest the tranquilzing action of maprotiline at work, probably forming a specific pharmcological feature of maprotiline. Also, maprotiline increases body weight of rats strikingly, which seems to offer a wide range of clinical applications of this drug. 13 references. (Author abstract)

231437 Peterson, Dale William. University of Minnesota **Functional significance of central nervous system norepinephrine and dopamine: a psychopharmacological study. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-21080 HC$13.50 MF$5.00 96 p.

The possible involvement of norepinephrine (NE) was separated from dopamine (DA) in the performance of conditioned behavior in rats. In the first group of experiments, the intraventricular injection of 200 micrograms of 6-hydroxydopamine (6-)HDA) was compared with the effects of an intraventricular injection of ascorbic acid saline vehicle in rats. Suppression of responding to a food reinforcment by several doses of amphetamine was not altered by 6-OHDA treatment, but the same action of l-amphetamine was significantly attenuated, indicating that l-amphetamine's behavioral action is more dependent on NE than is that of d-amphetamine. The second group of experiments measured the metabolites of 3H-ne and 3H-DA in a lateral ventricular perfusate of a rat performing a conditioned response and the effects of d-amphetamine and l-amphetamine on that response. Results are discussed in relation to possible differences in the mechanisms by which d-amphetamine and l-amphetamine alter NE in the brain. (Journal abstract modified)

231533 Kelfer, Deborah Ann. University of Illinois at Chicago Circle **Effects of methylphenidate on auditory intensity discrimination and generalization in the immature rat. (Ph.D. dissertation).** Disertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-23359 HC$13.50 MF$5.00 72 p.

The effect of methylphenidate, a central nervous system stimulant, was examined in discrimination and generalization situations in order to assess its action on auditory stimulus control. Methylphenidate reduced operant response rates and significantly impaired performance of an auditory intensity discrimination task in immature rats. Conditions in which auditory intensity of S minus was greater than S plus also reduced response rates and discrimination performance. In generalization testing along the auditory intensity continuum, drug injections significantly reduced response rates without significantly altering the slope of the generalization gradient. Generalization gradients were significantly steeper after discrimination training with S plus of higher intensity than S minus. Both drug and lower intensity S plus training conditions reduced generalization response rates. The flattest gradients were obtained when Ss were drugged in both training and testing and when they were trained with lower intensity S plus conditions. Drugs did not produce state dependent or rate dependent effects. Neither drug nor its intensity conditions differentially affected the appearance of peak shift. Results are interpreted in terms of drug induced hyperactivity and stimulus intensity dynamism. (Journal abstract modified)

231707 Larkin, Ronald P. Rockefeller University, 1230 York Avenue, New York, NY 10021 **Effect of ventromedial hypothalamic procaine injections on feeding, lever pressing, and other behavior in rats.** Journal of Comparative & Physiological Psychology. 89(9):1100-1108, 1975.

The effect of ventromedial hypothalamic (VMH) procaine injections on feeding, lever pressing, and other behavior was studied in Wistar rats. Rats were given bilateral injections of 1-2 microliters of procaine HCl solution (50 micrograms/microliter) in the region of the VMH. Normal sized meals occured reliably with a latency of 16 sec to 120 sec, indicating that this region has the function of inhibiting onset of eating, not just the function of stopping a meal. Food rewarded fixed-ratio of one (FR 1; continuous reinforcement)

lever pressing was elicited by 2 microliters but not by 1 microliter of procaine. The FR 64 pressing was disrupted during a period of increased activity following procaine injection, although visual observations indicated that the pressing which did occur was normal in topography and was significantly associated in temporal sequence with approaches of the food magazine. 35 references. (Author abstract)

231771 Post, Robert M.; Kopanda, Richard T.; Lee, Arison. Section on Psychobiology, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Progressive behavioral changes during chronic lidocaine administration: relationship to kindling. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 7 p.

In a study of behavior changes during chronic lidocaine administration, five times weekly administration of lidocaine (60mg/kg) caused the progressive development of abnormal eating behavior and seizures. Experimental rats became omniphagic, eating significantly more feces, straw and gauze than controls. Following an average of 15 lidocaine injections unassociated with seizures, animals began to have major motor convulsions which increased in frequency and duration. A pharmacological kindling mechanism is suggested for the progressive effects of lidocaine on behavior and seizures. 30 references. (Author abstract modified)

232332 Olds, M. E. California Institute of Technology, Division of Biology, Pasadena, CA 91125 **Effects of intraventricular 6-hydroxydopamine and replacement therapy with norepinephrine, dopamine, and serotonin on self-stimulation in diencephalic and mesencephalic regions in the rat.** Brain Research (Amsterdam). 98(2):327-342, 1975.

The effects of intraventricular 6-hydroxydopamine (6-OHDA) and replacement therapy on self-stimulation were studied in rats implanted with rewarding probes in the hypothalamus, the substantia nigra, the midbrain, and the pontine region. Two patterns of self-stimulation emerged in each subject. A pattern characterized by short, medium and long stimulus train durations was seen in the hypothalamus, substantia nigra and selected sites in the pons. A pattern of only short stimulus trains was found in the medial midbrain and in the pontine region. 6-OHDA reduced rate of responding in regions where responding was for short, medium and long stimulus trains. It had a minor effect in regions where rewards were exclusively of short duration. L-Norepinephrine injected in the lateral ventricle of 6-OHDA treated rats temporarily reinstated self-stimulation in the lateral hypothalamus but not in the substantia nigra and the pontine region. Dopamine was not effective in antagonizing the suppressant action of 6-OHDA. Serotonin reinstated self-stimulation in the lateral hypothalmus, but its action was less effective than that of norepinephrine. 49 references. (Author abstract modified)

232483 Romaniuk, Andrzej; Brudzynski, Stefan; Gronska, Jolanta. Zaklad Fizjologii Zwierzat Instytutu Fizjologii i Cytologii Uniwersytetu Lodzkiego, 90-222 Lodz, Rewolucji 1905 r. 66, Poland **Comparison of defensive behavior evoked by chemical and electrical stimulation of the hypothalamus in cats.** Acta Physiologica Polonica (Warszawa). 26(1):23-31, 1975.

Defensive behavior evoked by chemical and electrical stimulation of the hypothalamus in cats is discussed. An injection of 5 micrograms of carbachol into the hypothalamus produced a rage reaction. Electrostimulation of the same hypothalamic area also produced rage. Experiments with carbachol injections and electrostimulation after blockade of the hypothalamic muscarinic receptors indicated that the rage reaction is evoked in different ways by the two methods. Data regarding localization of the hypothalamic centers responsible or certain types of defensive reactions are discussed. 42 references. (Author abstract modified)

232484 Herman, Zbigniew S. Zaklad Farmakologii IBF, Sl. AM 41-808 Zabrze, Marksa 38, Poland **Behavioral effects of dibutyryl cyclic 3'5'AMP and biogenic amines in rats.** Acta Physiologica Polonica (Warszawa). 26(1):109-112 1975.

The influence of dibutyryl cyclic 3',5'-AMP (DAMP) on the behavior effects of dopamine (DA), 5-hydroxytryptamine (5-HT), and acetylcholine (ACh) was examined. White male Wistar rats were injected intraventricularly with 200 micrograms of some of the DAMP. Thirty min later animals were injected intraventricularly with 10 micrograms of DA, 10 (5HT) or 50 of ACh. Immediately after injection of the amines the time of waking, convulsions, immobility and number of jumps during 10 min periods of observations was measured. It was found that DAMP induced excitation in animals, expressed by convulsions, jumping and short periods of immobility; all studied biogenic amines inhibited convulsions and caused periodically stereotypical behavior; 5-HT and ACh increased the time of immobility in animals injected with DAMP; DA increased jumping behavior. Results indicate the interaction between DAMP and DA and 5-HT and ACh on behavioral phenomena in rats. 11 references. (Author abstract modified)

232509 Cook, Leonard; Sepinwall, Jerry. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Behavioral analysis of the effects and mechanisms of action of benzodiazepines.** In: Costa, E., Mechanism of action of benzodiazepines. New York, Raven Press, 1975. 181 p. (p. 1-28).

The antianxiety activity of the 1,4-benzodiazepines chlordiazepoxide and diazepam is reviewed, and behavioral methods which have contributed to identifying this activity and to exploring mechanisms of action hypotheses are described. Research is presented in which conflict behavior in animals was used to evaluate several biochemical hypotheses concerning antianxiety action of benzodiazepines, based on inhibition of cyclic 3',5'-adenosine monophosphate or the involvement of serotonin, gamma-aminobutyric acid, or glycine. The relationship of the results of this analysis to prediction of clinical antianxiety activity is discussed, and it is concluded that conflict behavior is a powerful tool in revealing relevant pharmacological correlates of the therapeutically desirable properties of benzodiazepine antianxiety compounds. 48 references.

232529 Janssen, P. A. J.; Niemegeers, C. J. E.; Schellekens, K. H. L.; Lenaerts, F. M.; Wauquier, A. no address **Clopimozide (R 29 764), a new highly potent and orally long-acting neuroleptic of the diphenylbutylpiperidine series.** Arzneimittel-Forschung (Aulendorf). 25(8):1287-1294, 1975.

Clopimozide (R-29764), 5-chloro-1-(4-(4,4-bis(p-fluorophenyl)butyl)-4 -piperidyl)-2-benzimidazolinone, a new member of the potent and orally long-acting series of diphenylbutylpiperidine neuroleptics was tested in mice, rats, guinea-pigs and dogs. In animals the pharmacological profile of R-29764 resembles that of typical neuroleptic compounds. R-29764 is very potent by oral route and has an extremely long duration of action. The onset of action of clopimozide is relatively fast; it is already very potent after 4hr and, in the procedures described, reaches its peak effect 24h after administration. In spite of the high potency and long duration of action, clopimozide is relatively atoxic. The safety margin, calculated as the ratio between the acute LD50 value and the lowest ED50 value is greater than 15.000 in rats and much greater than 7.250

in dogs. Qualitatively, R-29764 is more closely related to haloperidol, pimozide and penfluridol than to chlorpromazine. The side-effect liability is expected to be very low when hypotensive, autonomic and undesirable neurological side-effects are concerned. 31 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

226848 Mendelson, Wallace B.; Cicero, Theodore J. Lab. of Clinical Psychopharmacology, NIMH, Bldg. 10, Room 3N224, Bethesda, MD 20014 **Possible role of the alpha-adrenergic system in narcotic withdrawal: toxic interaction between methadone and phenoxybenzamine. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 6 p.

Possible toxic effects of phenoxybenzamine in methadone addicted rats were tested. Rats were divided into three groups: methadone - saline, phenoxybenzamine, and methadone - phenoxybensamine. The results show that there were significantly more frequent deaths in the methadone - phenoxybenzamine group than in either of the other two groups. Thus, although an earlier animal study suggested that phenoxybenzamine may block some signs of narcotic withdrawal, the toxic interaction observed in this study would seem to contraindicate the use of phenoxybenzamine in treating human addicts. 8 references.

226944 Lefkowitz, Stanely S.; Chian, Chinlee Yang. Department of Microbiology, Texas Tech University School of Medicine, Lubbock, TX 79409 **Effects of delta-9-tetrahydrocannabinol on mouse spleens.** Research Communications in Chemical Pathology and Pharmacology. 11(4):659-662, 1975.

The effects of delta9-tetrahydrocannabinol (THC) on the plaque forming cell response of mice immunized with sheep erythrocytes were examined. It was found that a marked suppression of plaque forming cells occurred concomitant with a general loss of spleen cellularity following administration of THC. These results suggest rather marked effects of this drug on antibody synthesis. 6 references. (Author abstract)

227391 Bourdois, P. S.; Junghani, J.; Perraud, J.; Reinert, H. Centre de Recherche Pfizer, 37400 Amboise, France **Transplacental effects of drugs on hearing, vision, and behaviour.** Toxicology and Applied Pharmacology. 33(1):196, 1975.

At the Fourteenth Annual Meeting of the Society of Toxicology, held at Williambsurg, Virginia, in March 1973, the transplacental effects of drugs on hearing, vision, and behavior in rats and cat were reported. The open field technique was used to measure two stereotype responses (ambulation and rearing) and emotion (defecation). Amphetamine, iproniazid chlorpromazine, pemoline, and monosodium glutamate were tested in 4-week-old rats. Preyer's reflex, elicited by audiometer generated sounds at threshold amplitude and different frequencies, was chosen to test hearing. Gentamicin, kanamycin, dihydrostreptomycin, and ethacrynic acid were examined in 25-day-old rats and guinea-pigs. Cats were used to test the effects on vestibular function. Vision was tested by recording stroboscope evoked cortical potentials. (Journal abstract modified)

228554 Yershova, V. P. Stavropol'skogo meditsinskogo instituta, Stavropol, U.S.S.R. **/The effect of chronic injections of chlorpromazine on oogenesis and progeny development in albino mice./** O vliyanii khronicheskikh in"yektsiy aminazina na oogenez i razvitiye potomstva zhivotnykh (belykh myshey). Farmakologiya i toksikologiya (Moskva). 38(4):473-476, 1975.

The effect of chlorpromazine on oogenesis and progeny development was investigated in albino mice subjected to chronic chlorpromazine injections during various stages of pregnancy. Chlorpromazine administration in doses of 16mg/kg prior to the onset of pregnancy was found to inhibit oogenesis, thus reducing the number of young mice in the litter. Chlorpromazine administration prior to pregnancy coupled with a single injection of the drug at the end of gestation was found to either interrupt the pregnancy or seriously disturb postnatal development of some of the offspring. Postnatal disturbances included: delayed growth and motor activity; lack of motion coordination; changes in skin; diarrhea; and underdevelopment of the organs and of their histological structures. 13 references. (Journal abstract modified)

228977 Roszell, D. K.; Horita, A. Riverview Hospital, Essondale, British Columbia **The effects of haloperidol and thioridazine on apomorphine- and LSD-induced hyperthermia in the rabbit.** Journal of Psychiatric Research (Oxford). 12(2):117-123, 1975.

The administration of LSD (100micrograms/kg) or apomorphine (4mg/kg) to male New Zealand rabbits resulted in a pronounced hyperthermic response accompanied by behavioral excitation and sympathetic activity. In addition, apomorphine exhibited several compulsive stereotyped responses, such as head turning and gnawing. Rabbits, which were pretreated with various doses of thioridazine or haloperidol, responded to LSD with slightly attenuated hyperthermia and behavioral excitation. The apomorphine induced responses were markedly attenuated or abolished with far smaller doses of the neuroleptics. The hyperthermic action of apomorphine was more sensitive to the actions of the antagonists than were the behavioral signs, total blockade being seen with 0.50mg/kg of thioridazine and 0.05mg/kg of haloperidol. The hyperthermic response to apomorphine thus represents a sensitive dopaminergic response, and may serve as a useful model in the evaluation of the antidopamine activity of the neuroleptic drugs. 15 references. (Author abstract)

231604 Sethi, N; Sethi, B. B. Central Drug Research Institute, Lucknow, India **A teratogenic study of haloperidol.** Indian Journal of Psychiatry (Madurai). 16(2):165-169, 1974.

The effects of administering haloperidol to pregnant rats on the offspring of those rats were examined to study the possibility of teratogenic side-effects. Pregnant female mice were divided into four treatment groups: the first three groups received haloperidol in doses of 2.5, 5, and 10mg/kg bodyweight respectively by gavage on gestation days 6 through 15 (the period of organogenesis). The fourth group served as control. All animals were delivered by caesarean section on the 20th day postcoitus. No visceral or skeletal deformities were found; but the implantation number was reduced and resorptions were high, reducing the litter size in drug treated animals. Litter size was markedly reduced in the highest dose group. Litter weight was significantly affected in the groups receiving 5 and 10mg/kg daily. It is concluded that haloperidol is embryotoxic and not teratogenic. 7 references.

06 METHODS DEVELOPMENT

227207 Simon, P.; Boissier, J. R. Paris **Evaluating potential anti-depressants in animals.** Journal of International Medical Research (Northampton). 3(Suppl. 3):14-17, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the process of evaluating potential antidepressants in animals was

described. The most commonly used tests were outlined, including those used to detect: antireserpine activity; anticataleptic activity; antagonism of central cholinergics; potentiation of effects of amphetamine and biogenic amines; and potentiation of yohimbine. It was stated that a substance which has these effects, especially if it does not produce any pronounced change in the behavior of normal animals may well have antidepressant effects in man. This spectrum of activity corresponds to that shown by the tricyclic antidepressants. Some practical problems connected with the use of models of depression (isolation, sensory deprivation, parent separation) were examined. (Author abstract modified)

227382 Myers, R. D. no address **Handbook of drug and chemical stimulation of the brain: behavioral, pharmacological and physiological aspects.** London, Van Nostrand Reinhold, 1975. 759 p. L19.90.

The practical difficulties and pitfalls of techniques for the direct administration of drugs into the cerebospinal fluid and into discrete areas of the central nervous system (CNS) are discussed. Particular problems with these techniques include the inability to control localization, the difficulty in estimating appropriate dosages, and the unwanted manifestations of the membrane stabilizing effects of many drugs. Further discussion includes the theoretical framework, principles and experimental methods of direct administration. Also discussed are the results obtained in attempts to manipulate a wide variety of bodily functions or behavioral states including sexual behavior, sleep, neuroendocrine relationships, arousal, pain and cognitive functions. It is noted that sophisticated methods do exist for the microapplication of drugs onto single neurons in the CNS by microiontophoresis.

227764 Collard, Jackie. Hopital de Baviere, Salle 44, Blvd. de la Constitution 66, B-4000, Liege, Belgium **The main clinical classifications of neuroleptics.** Acta Psychiatrica Belgica (Bruxelles). 74(5):447-461, 1974.

At the first joint meeting of the Scandinavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the various classification systems of neuroleptics were discussed. The classification schemes of Lambert, Pichot, and Delay and Deniker were described, and the development of the Liege physiognomy was detailed. The clinical physiognomy of phenothiazines, butyrophenones, thioxanthenes, dibenzothiazepines, ethylaminoindols, azaphenothiazines, and benzamides were illustrated.

229429 Dews, P. B. Psychiatry Department, Laboratory of Psychobiology, Harvard Medical School, Boston, MA **Strategies of basic research in development of drugs.** Psychopharmacology Bulletin. 11(4):6-7, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 strategies of basic research in the development of drugs, including those for use in psychiatry, were reviewed, stressing that in spite of the fact that new and valuable therapeutic agents have been formulated in recent years, the public is still skeptical. It was pointed out that this skepticism is due to discrepancies between what is actually done in practice and what is reported: 1) attributing many discoveries as serendipitous, suggesting that researchers are groping around randomly; 2) the reported use of animal models for research without fully describing the conditions under which they are used and the species which are included; 3) the manner in which new drug evaluations with human subjects are handled, often implying the chance of high-risk where risk is not indicated. 1 reference. (Journal abstract modified)

229493 Shillady, Donald D. Virginia Commonwealth University, Richmond, VA 23220 **Magnetic circular dichroism of substituted indoles.** Psychopharmacology Bulletin. 11(4):77, 1975.

A highly sensitive spectrometer is being developed to measure circular dichroism induced by a powerful magnetic field for use in analytical detection procedures and monitoring in enzyme kinetic studies of biochemicals and psychopharmacological agents containing the indole moiety. Magnetic circular dichroism (MCD) offers a number of advantages over other techniques: no fractionation is necessary and immediate direct measurements can be made speedily and economically. The time averaged MCD spectra of serotonin and its biosynthesis in cockroaches and white rats are measured from L-tryptophan via 5-hydroxytryptophan, followed by degradation of 5-hydroxyindole acetaldehyde and 5-hydroxyindoleacetic acid. The kinetics of these enzymic reactions are studied in vitro by noting changes in the MCD spectra. A minicomputer is interfaced to perform time averaging scanning. Studies with related compounds, such as psilocyn and 5-hydroxytryptophol, involve analysis of electronic effects of chemical substitution of the parent compound as manifested in the MCD spectra. Fluorescence and ultraviolent spectroscopy are used to check the analytical results and augment the electronic interpretations. (Journal abstract modified)

230877 Muizelaar, J. P.; Oberink, J. I. Netherlands Central Institute for Brain Research, Ijdijk 28, Amsterdam, Havens Oost, The Netherlands **Probenecid: dosage, levels in plasma and cerebrospinal fluid (CSF) and influence upon CSF levels of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in the rabbit.** Psychopharmacologia (Berlin). 43(3):223-227, 1975.

Correlations between administered doses of probenecid and levels in plasma and cerebrospinal fluid (CSF) and the correlation between levels of probenecid and homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in CSF were examined in rabbits. Probenecid retards the efflux of acid monoamine metabolites from the brain tissue and CSF to the blood. The probenecid induced accumulation of these metabolites is held to be indicative of the turnover rate of the corresponding amines. All correlations proved to be significant. The implications of these results for studies using the probenecid technique are discussed. 33 references. (Author abstract modified)

231072 Tonkopiy, V. D.; Prozorovskiy, V. B.; Konstorum, M. G. Voyenno-meditsinskaya akademiya im. Kirova, Leningrad, U.S.S.R. **/A simple method of evaluating the competitive interaction of reversible inhibitors with cholinesterases./** Prostoy metod otsenki konkurentnosti vzaimodeystviya obratimykh ingibitorov s kholinesterazami. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 80(8):120-122, 1975.

A method for determination of the extent of the competitive interaction of the reversible inhibitors with cholinesterases is described. The method is based on comparison of the 150 values determined by various commonly accepted methods. Although this method cannot serve as a replacement for kinetic investigation, it is effective in measuring the interaction of reversible inhibitors with cholinesterases in the presence of a substrate. 7 references. (Journal abstract modified)

231278 Meek, James L. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Inexpensive equipment for high pressure liquid chromatography: application to assays for taurine, gamma-amino butyric acid and 5-hydroxytryptophan. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 26 p.

An inexpensive pump is described for high pressure liquid chromatography which can be assembled from readily available parts. The pressurized tank type apparatus can be used with conventional liquid chromatography detectors or with the spectrophotometers or fluorometers available in most laboratories. The system has been applied to the measurement of specific amino acids in brain tissues: taurine, gamma-aminobutyric acid and 5-hydroxytryptophan. The assays, which can measure less than 50 pmol, require only 3 to 7 minutes per sample and require no sample preparation other than precipitation of proteins. The apparatus can perform complex separations for analytical work; but its simplicity, high speed and ease of sample preparation make it also suitable for enzymatic and clinical studies. 19 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

226430 Mattsson, B.; Bertilsson, L. Dept. of Psychiatry, University of Umea, S-901 85 Umea, Sweden **Treatment with disulfiram in Huntington's chorea: a negative clinical and pharmacological study.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:261-268, 1974.

Disulfiram administered in moderate doses for 4 weeks to five patients with Huntington's chorea produced a slight increase in choreic movements in two patients. No changes were observed in homovanillic acid, 5-hydroxyindoleacetic acid, indoleacetic acid, and 4-hydroxy-3-methoxyphenyl-glycol in cerebrospinal fluid, nor in dopamine-beta-hydroxylase in plasma and homovanillic acid in serum. It is suggested that the negative result is due to too low doses of disulfiram. 14 references. (Author abstract modified)

227210 Turner, P.; Bayliss, P. F. C.; Ghose, K. Department of Clinical Pharmacology, St. Bartholomew's Hospital, London **Clinical pharmacology of viloxazine (Vivalan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):41-49, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the effects of viloxazine, an antidepressant with a new chemical structure, were discussed with respect to anticholinergic activity, adrenergic activity and central effects. Double-blind tests of viloxazine against imipramine in healthy volunteers revealed no anticholinergic effects with viloxazine. In doses of up to 300mg/day for one week, viloxazine showed no evidence of blocking the tyramine pressor response in contrast to amitriptyline. Using critical flicker frequency and reaction time, there appeared to be little or no central effects of viloxazine. 7 references. (Author abstract modified)

227212 Goodwin, B. L.; Johnson, R. D.; Ruthven, C. R. J.; Sandler, M. Queen Charlotte's Maternity Hospital, London **Effect of viloxazine (Vivalan) on the urinary excretion of catecholamines and their metabolites.** Journal of International Medical Research (Northampton). 3(Suppl. 3):57-61, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study of the urinary excretion of catecholamines and their metabolites in the human before and during dosage with 100mg twice daily viloxazine (Vivalan) was reported. The first trial involved 12 normal volunteers, in whom free 5-hydroxyindoleacetic acid (5-HIAA), free and total catecholamines, and their metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) (total and free), homovanillic acid (HVA) (free), 4-hydroxy-3-methoxymandelic acid (VMA) (free) and 4-hydroxy-3-methoxyphenylglycol (HMPG) (total) were measured by gas chromatography on 24 hr urine samples. Free and total DOPAC and free 5-HIAA were estimated in the 10 normal subjects taking part in the second trial. There was a significant decrease in urinary DOPAC (free and total), HVA and VMA while on viloxazine, expressed both in terms of 24 hr output and in relation to creatinine excretion. There were no consistent changes in amine output. In contrast to findings in the first group, the second showed no change in the 24 hr output of free and conjugated DOPAC; on the basis of creatinine excretion there was a significant fall during the administration of viloxazine. In neither trial was there any effect on the urinary output of 5-HIAA whether calculated as mg per 24 hr or per g creatinine. 11 references. (Author abstract modified)

227219 Amaducci, L. Florence, Italy **Multicentre studies with viloxazine (Vicilan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):95-96, 1975.

At the International Vivalan Symposium, held in London in November 1974, preliminary data from a multicenter trial of viloxazine (Vicilan) were reported. Data relate to 53 inpatients, 20 of whom took part in an open study and 24 in a double-blind trial against imipramine. Changes in mood were measured by the Hamilton rating scale and a self-rating scale frequently used in Italy, the Gainotti-Cianchetti. In the open study 18 patients continued throughout the 4 week period with a significant improvement on the Hamilton scale after 1 week. In the early stages some patients complained of palpitation and asthenia. In the double-blind trial there was significant improvement with both viloxazine and imipramine after 2 weeks and after 4 weeks viloxazine appeared to be better than imipramine. When the data were studied on the self-rating scale, viloxazine was clearly better than imipramine. Nausea was present in two cases initially but this disappeared after 4 weeks. It was concluded that viloxazine is the treatment of choice because, with its low side-effects, it can be used where anticholinergic effects are undesirable.

227227 Murphy, J. E. Clinical Research International, Northampton, England **Vivalan: drug profile.** Journal of International Medical Research (Northampton). 3(Suppl. 3):122-124, 1975.

At the International Vivalan Symposium, held in London in November 1974, reports of early clinical trials of the drug viloxazine (Vivalan) were summarized. Vivalan is a new psychotropic compound which has a bicyclic structure containing an oxazine nucleus. From a synthesis of the reports presented, it was concluded that Vivalan is an effective antidepressant and that its onset of action is relatively fast, probably occurring in some instances in the first 2 days of treatment. It was noted that the drug is better tolerated than imipramine, in that it has fewer side-effects and less persistent side-effects. It was also stated that the classical sedative and anticholinergic properties of the tricyclic antidepressants are virtually absent with Vivalan, but that in their stead the drug produces upper gastrointestinal disturbances in up to 18% of cases. However, it was maintained that this occurs relatively early in treatment and is transient in its duration.

229026 Inanaga, Kazutoyo; Arikawa, Katsuyoshi; Kitahara, Takayoshi; Yamazaki, Tatsuo; Shibata, Doji; Yamaguchi, Eiich; Kai, Yasunobu; Inoue, Kazuzo. Department of Neuropsychiatry, Kurume University School of Medicine, Japan **A double blind comparison of penfluridol (easer) with pimozide in schizophrenia.** Clinical Psychiatry (Tokyo). 17(3):287-298, 1975.

The effect of penfluridol (Pe) and pimozide (Pi) on schizophrenia was studied, based on a double-blind experienment in which 133 schizophrenic patients were treated with either Pe or Pi for 8 weeks. Pe was extremely to moderately effective in 77.2% of the patients, and Pi in 57.9%. Among those patients with more than 3 years of schizophrenic history, Pe was more effective than Pi. Pe was also more effective with hebephrenia. No significant differences between the two drugs was observed in their effects on catatonic and paranoic

type of schizophrenia. Pe was more effective than Pi in treating hallucinations, and disturbances in self-awareness, but no significant differences were observed between the two drugs in their effects on other schizophrenic symptoms. 14 references.

229036 Weliky, I.; Neiss, E. S. Dept. of Clinical Pharmacology, Division of Medical Affairs, Squibb Institute for Medical Research, Princeton, NJ 08540 **Clinical pharmacology of SQ-10996, a potential antidepressive agent.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):252-257, 1975.

Studies were undertaken to determine the tolerance of healthy human subjects of SQ-10996, a potential antidepressive agent. Single oral doses of the drug ranging from 500mg to 1000mg were given once daily for three consecutive days to groups of healthy subjects and were well tolerated. One of three subjects given 1250mg and two of three subjects given 1500mg became drowsy on the second and third day; this symptom disappeared within 24 hours after cessation of dose. A short-term, multiple dose tolerance study was carried out with a formulation of SQ-10996, the bioavailability of which was comparable to that of the formulation used in the ascending dose study. When 200mg doses were administered every 12, 8, or 6 hours over a 6 day period, mean steady state serum concentrations of approximately 4, 7, and 8 micrograms/ml were attained within 48 hours; no subject showed any sign of drowsiness. The half-life for SQ-10996 in serum, estimated from concentrations in serum after the last dose, was approximately 13 hours, significantly shorter than the half-life found after the administration of single 10mg doses. Findings show the drug to be biologically available and well tolerated. 5 references. (Author abstract modified)

229038 Itil, T, M.; Herrmann, W. M.; Akpinar, S. Division of Biological Psychiatry, Dept. of Psychiatry, New York Medical College, New York, NY **Prediction of psychotropic properties of lisuride hydrogen maleate by quantitative pharmaco-electroencephalogram.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):221-233, 1975.

The use of the quantitative pharmaco-electroencephalogram (EEG), a new method of early clinical drug evaluation, is described, and the use of computer analyzed EEG (CEEG) measurements to predict central nervous system (CNS) effects of lisuride hydrogen maleate (LHM) is reported. CEEG profiles of LHM in low dosages (10 micrograms) are similar to those of CNS inhibitory compounds, while in higher dosages (25 micrograms to 100 micrograms) they resemble profiles of psychostimulant compounds. By measuring the brain function using computer period analysis of cerebral bipotentials, dose efficacy relations were found (in the range of 25-75 micrograms) which suggest the bioavailability of LHM at the CNS level. By comparing the CEEG profiles of LHM with the previously studied compounds, five different clinical uses of LHM were predicted. The pilot trials suggest that LHM may have therapeutic potentials in patients with "aging" and/or organic brain syndromes and in children with behavioral disturbances. 18 references. (Author abstract modified)

232530 Babbini, M.; Torrielli, M. V.; Strumia, E.; Gaiardi, M.; Bartoletti, M.; De Marchi, F. no address **Sedative-hypnotic properties of a new benzodiazepine in comparison with flurazepam: pharmacological and clinical findings.** Arzneimittel-Forschung (Aulendorf). 25(8):1294-1300, 1975.

The sedative/hypnotic effects of a new benzodiazepine, 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1,3-dihydro-5-(o-fluorophenyl) -2H-1,4-benzodiazepin-2-one (SAS-643), were compared with those of flurazepam in mice and rats and in a double-blind clinical trial. It was found that SAS-643 has a potency 2 to 4 times greater than that of flurazepam, while it is about one half less toxic than the latter drug. The results of the clinical trial confirm the greater activity of SAS-643 and indicate that the new benzodiazepine causes significantly less hangover than does flurazepam. 18 references. (Author abstract)

08 DRUG TRIALS IN SCHIZOPHRENIA

225826 Feinsilver, David B.; Gunderson, John G. no address **Psychotherapy for schizophrenics: is it indicated?** In: Gunderson, J., Psychotherapy of schizophrenia. New York, Jason Aronson, 1975. 441 p. (p. 403-430).

Five research studies on therapeutic methods used for schizophrenics are reviewed; methods discussed are psychotherapy alone, psychotherapy plus drugs, drugs alone, electroconvulsive therapy, and milieu therapy alone. It is felt that while results neither proved psychotherapy ineffective nor provided any strong evidence of its helpfulness, substantial advances in methodology have occurred as one result of the studies, including suggestions for study criteria and patient progress scales. Studies are considered to confirm drug literature in demonstrating the efficacy of drugs in acute schizophrenia, but the more global question of the value of psychotherapy was not seen as conclusively answered. Suggestions are made for designing more effective comparative studies. 34 references.

225867 Schiele, B. C. Department of Psychiatry, University of Minnesota Medical School, Minneapolis, MN **Loxapine succinate: a controlled double-blind study in chronic schizophrenia.** Diseases of the Nervous System. 36(7):361-364, 1975.

Loxapine succinate was compared to chlorpromazine in a 12 week double-blind study of 50 hospitalized chronic schizophrenic patients. Statistical analyses of BPRS (Brief Psychiatric Rating Scale) scores showed significant improvement for several items and factors in both groups of patients. Both drugs significantly decreased severity of illness on the CGI (Clinical Global Impression) scale. On the NOSIE (Nurses Observation Scale for Inpatient Evaluation) scale, manifest psychosis was improved significantly with chlorpromazine and global severity with loxapine succinate. There were no significant treatment differences in BPRS, CGI, or NOSIE items or in the reduction of overall psychopathology. The side-effects associated with the study drugs differed little with respect to incidence, number, severity, and type. The most frequently reported symptoms in both groups were behavioral, extrapyramidal, and sedative. Analyses of vital signs and clinical laboratory data revealed no evidence of serious untoward effects. 14 references. (Author abstract)

225932 Gottschalk, Louis A.; Biener, Robert; Noble, Ernest P.; Birch, Herman; Wilbert, Donald E.; Heiser, Jon F. Department of Psychiatry and Human Behavior, University of California at Irvine, Irvine, CA **Thioridazine plasma levels and clinical response.** Comprehensive Psychiatry. 16(4):323-337, 1975.

The relationship of a single, standardized oral dose of a phenothiazine derivative (thioridazine) to the resulting drug blood levels and clinical responses in acute schizophrenic patients was examined. Following the single dose of thioridazine in 25 patients with severe to moderately severe acute schizophrenia, a significant average decrease was noted within 24 hours in the social alienation/personal disorganization

scores and within 48 hours in various psychiatric rating scales. The manifestations of the schizophrenic syndrome showing significant improvement included thought disorder, conceptual disorganization, apathy, anxiety, and depression. Significant correlations were found between indices of plasma thioridazine levels and favorable clinical responses on certain behavioral and psychologic features of the schizophrenic syndrome. Suggestive evidence was obtained which points to some predrug behavioral and clinical laboratory data that may serve as predictors of thioridazine pharmacokinetics. 28 references. (Author abstract modified)

225935 Doust, J. W. Lovett; Huszka, Louis; Doust, Jonathan N. Lovett. Department of Psychiatry, University of Toronto, Toronto, Canada **Psychotropic drugs and gender as modifiers of the role of plasma tryptophan and serotonin in schizophrenia.** Comprehensive Psychiatry. 16(4):349-355, 1975.

A group of chronic schizophrenic patients controlled for psychotropic drug intake and a comparable group of healthy subjects whose plasma tryptophan and plasma serotonin levels reflect the metabolic turnover lacking in most previous studies were investigated. In a comparison of the total population plasma tryptophan results in 62 males with those of 55 females, a t-test showed no difference between the means of these groups. However, a comparison between the similarly heterogeneous 42 male and 33 female plasma serotonin means indicated a significantly lower level for the females. Older males of the control group had a higher plasma tryptophan level than did the older females, while a similar disparity for plasma serotonin was found between the sexes for younger healthy subjects. Similar trends were noted in the untreated patient group. Results show that untreated schizophrenic patients of both sexes have a significantly lower level of plasma tryptophan than a comparable group of healthy subjects. 38 references.

225936 Verhaegen, J. J. Psychiatric Hospital St. Bavo, Noordwijkerhout, The Netherlands **The long-term use of high doses of fluphenazine enanthate and fluphenazine decanoate.** Comprehensive Psychiatry. 16(4):357-362, 1975.

Seventy two patients, mostly chronic schizophrenics refractory to other treatments, were given fluphenazine enanthate of fluphenazine decanoate in doses ranging from 1 ml every 3 weeks to 5 ml every week. Electrocardiograms, ocular examinations, and blood chemistries were performed on those given the highest doses. Long-term treatment with high doses revealed no untoward toxic effect or evidence of accumulation. These difficult patients were well controlled on the injections, occasionally supplemented with oral medication. The need for flexibility of dosage is stressed. 13 references. (Author abstract)

226408 Agrup-Andersson, L.; Bengtsson, A.; Erlandsson, K.; Gottfries, C. G.; Witzell-Ostlund, G. Ostra Sjukhuset, S-212 24 Malmo, Sweden **Flupenthixol decanoate -- controlled investigation concerning dosage.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:7-14, 1974.

An investigation is reported comparing the therapeutic effects obtained when flupenthixol decanoate was given with different intervals between injections to 57 female patients, mainly schizophrenic. The patients were randomly divided into two groups. In one group, treatment with flupenthixol decanoate was continued as before, with one injection every 2 weeks and no change in dosage; the other group was given continued injection treatment every 2 weeks, but at every other injection active substance was replaced by placebo, thus reducing the dose per unit to half by prolonging the intervals between the injection of active substance. After 6 months no significant difference in clinical effect could be detected between the two treatment groups. In a few patients however, deterioration was recorded, which may have been due to the reduced dosage. It is recommended that flupenthixol decanoate be given in a dose of 2 ml.=40 mg. every fourth week. The investigation supplies no information about the doses required in the initial phase of treatment. 10 references.

226409 Gottfries, C. G.; Green, L. Dept. of Psychiatry, University of Umea, S-901 85 Umea, Sweden **Flupenthixol decanoate - in treatment of out-patients.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:15-24, 1974.

A followup study is presented that was conducted on 128 consecutive ambulatory patients, mostly schizophrenic, treated with depot flupenthixol decanoate. The relapse frequency during treatment with flupenthixol decanoate was significantly lower than before treatment, although all the patients were also being treated with neuroleptics before depot treatment was instituted. A higher relapse frequency was discovered among those patients who discontinued treatment than among those with treatment in progress. Of the patients with schizophrenia, 43% discontinued treatment. In 13% the drug was discontinued on doctor's orders, while in 14% the patients refused to appear for treatment and in 5% side-effects led to discontinuation of treatment. 6 references. (Author abstract modified)

226412 Jacobsson, L.; Noren, M.-B.; Perris, C.; Rapp, W. Dept. of Psychiatry, University of Umea, S-901 85 Umea, Sweden **A controlled trial of clothiapine and chlorpromazine in acute schizophrenic syndromes.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:55-70, 1974.

A study is reported of 49 psychotic hospitalized patients suffering from schizophrenic syndromes entered on a one month controlled trial of clothiapine and chlorpromazine. Ratings of symptoms before, during, and at the end of the study showed significant overall improvement as expressed by total scores. Improvement was found to concern mainly splitting, delusions, hallucinations and influence of thought, those factors composed of symptoms which commonly occur in the course of schizophrenic syndromes. Both drugs produced an improvement in the patients' behavior in the ward, and both drugs produced side-effects of initial tiredness and obstipation. 15 references. (Author abstract modified)

227765 Holden, J. Mike C. Nesfield Hall, Nesfield, N. Inkley, Yorkshire, England **Clinical and electroencephalographical studies of the thioxanthenes.** Acta Psychiatrica Belgica (Bruxelles). 74(5):526-528, 1974.

At the first joint meeting of the Scandinavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the results of clinical and electroencephalographic (EEG) studies of the effects of thioxanthenes in schizophrenics were reported. Tiotixene and flupentixol compared favorably with with trifluoperazine and fluphenazine, respectively, in the treatment of schizophrenia and management of depression. The thioxanthenes are well tolerated; extrapyramidal and depressive side-effects were minimal.

227767 Vranckx, Constant H. Veldbondstraat, B-3300, Tienen, Belgium **Pharmacokinetics of flupentixol decanoate.** Acta Psychiatrica Belgica (Bruxelles). 74(5):529-532, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the results of a study of the relationship between the absorption, diffusion and metabolism of flupentixol decanoate and its therapeutic activity in chronic schizophrenics were reported. The measurment of total serum and cerebrospinal fluid radioactivity indicated higher drug levels in bad therapy responders than in good responders, as well as a better relationship between drug levels and the handwriting area in bad responders than in good responders.

227770 Gottfries, Carl G. Umea Universitet, Psykiatriska Institutionen, S-901 85 Umea, Sweden **Flupentixol and flupentixol decanoate, with special reference to their antipsychotic effect.** Acta Psychiatrica Belgica (Bruxelles). 74(5):507-515, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the use of flupentixol and flupentixol decanoate with schizophrenics was reported. In one study patients received flupentixol for 3 months and then trifluoperazine for 3 months. The results indicate no significant differences between the two. Both have antipsychotic effects. Some variables indicate that flupentixol could be a little less ataraxic and the improvement in manual speed was also more evident in the flupentixol group. A study involving the administration of flupentixol decanoate to outpatients indicates it has the following advantages: 1) simple administration; 2) dose reduction; 3) earlier discharge; 4) greater efficacy; and 5) more success with patients who forget medication or lack motivation.

227771 De Buck, Rene P. Unite de Recherches psychopharmacologiques Institut de Psychiatrie, Place Van Gehuchten 4, B-1020, Brussels **Antiautistic effect of flupentixol.** Acta Psychiatrica Belgica (Bruxelles). 74(5):520-525, 1974.

At the first joint meeting of the Scandinavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, studies of the effects of flupentixol were reviewed. The results indicate that it has antidepressant as well as antiautistic effects. With schizophrenic patients, flupentixol helped decrease fatigue, autism and negativism and improved mood. The antiautistic properties of other neuroleptics were also discussed.

227821 Aguilar, Santiago J. Central Georgia Regional Hospital, Central State Hospital, Milledgeville, GA 31061 **An open study of mesoridazine (Serentil) in chronic schizophrenics.** Diseases of the Nervous System. 36(9):484-489, 1975.

Mesoridazine besylate (MB) was evaluated in an 8 week open label trial in 12 male and 41 female patients with chronic schizophrenia. After a 10 day drug free period the patients received MB in i.m. doses of 25-150mg/day on the first 10 study days, followed by daily tablet doses ranging from 25-400mg until the final day of the study. The Nurses' Observation Scale for Inpatient Evaluation (NOSIE) ratings showed that the patients were significantly less mentally ill at the end of the drug free period and underwent a highly significant further improvement in the course of the MB treatment. These improvements occurred in irritability, manifest psychosis, retardation, depressive manifestations, and social competence. MB treatment also led to improvement in thinking disturbances and in psychomotor, paranoid and depressive disturbances. Patients in a subgroup of depressive disturbances showed significantly greater improvement than patients in another subgroup, psychomotor disturbances. Adverse reactions were experienced by a total of 13 patients; in 7 of these a dosage adjustment was necessary. 6 references. (Author abstract modified)

228068 Chang, Hwan-Il; Shin, Young-Woo. Department of Neuro-Psychiatry, Medical College, Kyung Hee University, Seoul, Korea **Schizophreniform psychosis of epilepsy: two cases with paroxysmal dysrhythmia on EEG.** Journal of the Korean Medical Association (Seoul). 17(11):870-876, 1974.

Two cases are reported which were diagnosed and treated as schizophrenia for more than 4 years and have not shown any improvement. Paroxysmal dysrhythmia was revealed on electroencephalograms, and anticonvulsant drugs were tried. Marked improvements in the schizophrenia like symptoms were noted. The two cases had histories of generalized convulsion at the age of 2 to 3 yers, which had disappeared spontaneously. Occasional episodic attacks of headaches and dizziness had occurred since the onset of mental symptoms, which also subsided with administration of the anticonvulsants. 39 references. (Journal abstract)

228221 Kellner, Robert; Wilson, Rogert M.; Muldawer, Michael D.; Pathak, Dorothy. Veterans Administration Hospital, Albuquerque, NM 87108 **Anxiety in schizophrenia: the responses to chlordiazepoxide in an intensive design study.** Archives of General Psychiatry. 32(10):1246-1254, 1975.

Six anxious schizophrenic patients who were maintained with phenothiazines participated in a double-blind intensive design study of chlordiazepoxide and placebo for 12 weeks or longer. There were substantial differences between patients in their responses to chlordiazepoxide: two patients experienced significant and conspicuous relief of distress and reduction of typical schizophrenic symptoms. In another patient the differences, although statistically significant, were clinically less striking. In the three remaining patients no differences were observed between responses to the two treatments except that one patient was more depressed with chlordiazepoxide than with placebo. It is suggested that there are at least two kinds of anxiety in schizophrenia. 47 references. (Author abstract modified)

228223 Quitkin, Frederic, Rifkin, Arthur; Klein, Donald F. Long Island Jewish-Hillside Medical Center, Hillside Division, PO Box 38, Glen Oaks, NY 11004 **Very high dosage vs standard dosage fluphenazine in schizophrenia: a double-blind study of nonchronic treatment-refractory patients.** Archives of General Psychiatry. 32(10):1276-1281, 1975.

In a 6 week double-blind comparison of the therapeutic efficacy of two doses of fluphenazine (F), 18 nonchronic treatment refractory patients received a very high dose (maximum 1200mg/day) of F and 13 patients received the standard dose (maximum 30mg/day). The patients were evaluated by means of the Inpatient Multidimensional Psychiatric Scale (IMPS) and the Clinical Global Impression, which were completed before and after the study. The patients who received the standard dose showed greater improvement on a variety of measures. Analysis of IMPS scores indicated that some patients taking the high doses had akinesia, an extrapyramidal side-effect that in part accounted for their inferior response. The results are compared with those of an earlier study, in which patients taking high doses of F showed greater improvement than those taking low doses. 7 references.

228224 Callahan, Edward J.; Alevizos, Peter N.; Teigen, James R.; Newman, Hilda; Campbell, Michael D. Camarillo-Neuropsychiatric Institute Research Program, Box A, Camarillo, CA 93010 **Behavioral effects of reducing the daily frequency of phenothiazine administration.** Archives of General Psychiatry. 32(10):1285-1290, 1975.

In a study of the behavioral effects of reducing the daily frequency of phenothiazine administration, 24 chronic female schizophrenics were assigned to two groups matched for alertness, after an 11 day baseline of behavioral observations. In the first treatment phase, the administration of phenothiazine medication of one group was switched from a multiple dose schedule (three to four times per day) to a single daily administration, while the total daily dosage was held constant. The second group continued on a multiple administration schedule for 11 days and then was switched to a single daily dosage. A multivariate analysis of variance showed that there was no overall effect due to the schedule change; however, preplanned t-tests showed transitory decreases in nonfunctional behavior. The results are discussed in terms of implications for the administration of phenothiazines and the experimental analysis of drug effects. 39 references. (Author abstract modified)

228225 Chouinard, Guy; Annable, Lawrence; Serrano, Manuel; Albert, Jean M.; Charette, Robert. Dept. of Research, INRS-SANTE, Hopital St.-Jean-de-Dieu, Montreal-Gamelin, Quebec, Canada H1N 1Z0 **Amitriptyline-perphenazine interaction in ambulatory schizophrenic patients.** Archives of General Psychiatry. 32(10):1295-1307, 1975.

In a double-blind, placebo controlled clinical study, lasting 12 weeks, 48 male and 48 female ambulatory schizophrenic patients were randomly assigned to one of four treatments: placebo; amitriptyline hydrochloride, 125mg/day; perphenazine, 20mg/day; or amitriptyline-perphenazine, 20mg/day. Treatment groups contained an equal number of male and female patients. Perphenazine alone or in combination was substantially more effective in reducing psychopathological disorder than was the placebo, but there was no evidence to indicate the superiority of the amitriptyline-perphenazine combination over perphenazine alone. Amitriptyline alone was not substantially better than placebo and could not be considered an efficacious medication for the maintenance treatment of these patients. Less response to treatment was made by patients with long-term records or prior hospitalizations. 48 references. (Author abstract modified)

228240 Rada, Richard T.; Donlon, Patrick J. Dept. of Psychiatry, School of Medicine, University of New Mexico, Albuquerque, NM 87106 **Depression and the acute schizophrenic process.** Psychosomatics. 16(3):116-119, 1975.

The depressive component of schizophrenia was examined in 18 decompensating and reintegrating schizophrenics involved in an outpatient phenothiazine study. The study was conducted to determine the therapeutic efficacy and safety of piperacetazine. The rating scales used included Early Clinical Drug Evaluation Unit forms, the Brief Psychiatric Rating Scale, the Clinical Global Impressions, and the Hamilton Rating Scale for Depression. The findings suggest that, for some chronic schizophrenic patients, exacerbation of an acute psychotic process is accompanied by significant depression, which occurs as an integral component of the schizophrenic episode. A number of possible sources of the depressive component are suggested. Phenothiazine therapy, accompanied by tricyclic antidepressants when necessary, was found to be effective in the treatment of the depressive component of schizophrenia. 20 references.

228308 Nagashi, Michio. Department of Neuro-psychiatry, Tokyo Medical and Dental University, Bunkyo-ku, Tokyo **Recent views in psychopharmacology: approach to schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1287-1292, 1974.

The literature on the relationship between schizophrenia and dopamine is reviewed. Mechanism of onset of extrapyramidal syndromes induced by neuroleptics, mechanism of action of neuroleptics, distribution pattern of dopamine in nerve endings, dopamine receptors, and the role of dopamine in the process of onset of amphetamine psychosis are considered. 24 references.

228324 Yamaue, Sakae. Department of Neuro-psychiatry, Osaka City University School of Medicine, Osaka, Japan **Effects of long-term application of penfluridol (TLP-607) for schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1353-1361, 1974.

The effect of penfluridol (TLP-607) on schizophrenia was studied. Ten schizophrenics were treated with penfluridol for 8 months to 2 years, with an effectivity rate of 50%. Administration of penfluridol caused improvement in physical movements, emotional state, and cognitive processes during the first 6 months of treatment, and improved hallucination, self-identification and hypochondriacal and neurotic complaints during the first year of treatment. Administration of this drug for more than 1 year improved interpersonal relationships, verbal communication and attitude in recreation or occupational therapy. Side-effects were observed in nine patients, including constipation, insomnia, headache, anxiety, irritation, dizziness, Parkinsonism and akathysia. Most of these side-effects were induced by dosages of more than 80mg/week, and disappeared after decrease in the dosage. 15 references.

228325 Yoshida, Toshihiko; Kimura, Shigeteru; Kusuhara, Tamotsu; Itonaga, Yoshiaki; Miyamoto, Hisao; Mukai, Takahisa; Hashiguchi, Kenjiro; Katsuno, Taro. Fukuoka Prefectural Dazaifu Hospital, Japan **Deuteropathy after stopping psychiatric medication for chronic schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1363-1366, 1974.

Deuteropathy after cessation of psychopharmacotherapy for chronic schizophrenia was studied. Sixty nine patients with this trouble, whose symptoms included lack of motivation and impaired communication and interpersonal relationships, were studied. Most of them had been hospitalized and received psychopharmacotherapy for more than 3 years. About 55% of the patients had some symptoms after termination of psychotropic drugs, including nausea, vomiting, loss of appetite, insomnia, wandering, and irritation. About 70% of the patients with these symptoms experienced them within 2 days after stopping psychotropic drugs. The occurrence of these symptoms was in proportion to the length of treatment. A higher occurrence of side-effects was observed among those patients with phenothiazine derivatives than those treated with butyrophenone derivatives. 12 references.

229064 Inanaga, Kazutoyo; Nakazawa, Yoichi; Inoue, Katsume; Tachibana, Hisayuki; Oshima, Masachika; Kotorii, Tatayu; Tanaka, Masatoshi; Ogawa, Nobuya. Dept. of Neuropsychiatry, Kurume University School of Medicine, Kurume, Japan **Doubel-blind controlled study of L-dopa therapy in schizophrenia.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 29(2):123-143, 1975.

On the basis fo data indicating that L-dopa used in small doses along with antipsychotic drugs is effective in improving lack of spontaneity, abulia, emotional blunting, disturbance of contact, and other symptoms of schizophrenia, a double-blind controlled study was conducted to confirm the effectiveness

of the drug. A total of 105 hospitalized schizophrenics were administered either L-dopa (300-300mg) or inert placebo in addition to conventionally used antipsychotic drugs for 8 weeks. In the L-dopa group, overall therapeutic result was rated as excellent in five cases, good in five cases, fair in 16 cases, unchanged in 24 cases, and worsened in 2 cases. Results indicate that only in the incidence of excellent response was the L-dopa group significantly higher than in the placebo group. Patients with a duration of illness of less than 5 years experienced symptomatic improvement significantly more frequently with L-dopa than with placebo, but there was no significant difference between the two groups for those who were ill for more than 5 years. Results suggest that a combined therapy with small doses of L-dopa and antipsychotic drugs is effective in the control of autistic manifestations of schizophrenia. 19 references. (Author abstract modified)

229444 Clark, Mervin L.; Kaul, Pushkar N. University of Oklahoma Health Sciences Center, Oklahoma City, OK **A preliminary report on clinical response and blood levels of chlorpromazine and its sulfoxide during chlorpromazine therapy in chronic schizophrenic patients.** Psychopharmacology Bulletin. 11(4):28-30, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 a 12 week double-blind, placebo controlled, two dose level clinical trial with chlorpromazine (CPZ) to determine differences in clinical response and blood levels during therapy in long-term institutionalized chronic schizophrenics was reported. Clinical behavioral changes were monitored with a variety of instruments and procedures, and detailed pharmacological analyses were made. Results of the behavioral measures indicate that patients can clearly be divided by response index into good, minimal, and poor responders. The second, fourth, and twelfth week zero hour (steady state) concentration of CPZ, along with those of chlorpromazine sulfoxide (CPZO) and CPZ/CPZSO ratio also yielded significant data. The CPZ concentrations were distinctly higher in the good responders compared to those in the poor and minimal responders. 2 references. (Journal abstract modified)

229445 Schooler, Nina R.; Sakalis, George; Chan, T. L. Psychopharmacology Research Branch, NIMH, Rockville, MD 20852 **Chlorpromazine metabolism and clinical response in acute schizophrenia: a preliminary report.** Psychopharmacology Bulletin. 11(4):30-33, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 results were reported from pharmacokinetic analyses of plasma levels of mesoridazine and its metabolites as related to clinical response in acute schizophrenic patients following a single intramuscular drug dose. On the first and sixth day predrug and seventh and eighth day postdrug, all Ss were assessed on three behavioral rating scales and compared with normal controls. Pharmacokinetic indices showed wide but nonsignificant individual variation between patients and normals. Significant decreases in all clinical measurs occurred within 24 h postdrug among schizophrenics, but not among controls. Significant improvement with drug plasma peak level or half-life procedures with both ultraviolet and gas chromatographic analyses occurred in anergia and somatic/hysteria scores. Not only mesoridazine, but its major metabolite, sulforidazine, following a single drug dose showed the pharmacokinetic clinical response correlations. The relevance of such single dose studies to continuous dose studies is discussed. 5 references. (Journal abstract modified)

229446 Gottschalk, L. A.; Dinovo, E.; Bierner, R. Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA **Plasma levels of mesoridazine and its metabolites and clinical responses in acute schizophrenia after a single intramuscular drug dose.** Psychopharmacology Bulletin. 11(4):33-34, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 a series of single and multiple dose trials on healthy volunteers, undertaken to elucidate the pharmacokinetic properties of chlordiazepoxide (Librium), was reported. Blood concentrations of chlordiazepoxide (CDX) and its two pharmacologically active metabolites, desmethylchlordiazepoxide (DMCDX) and demoxepam (DMX) were determined. In addition, the influence of an antacid preparation on bioavailability of oral CDX was tested in healthy male volunteers, and the pharmacokinetics of CDX and its metabolites during chronic CDX therapy were studied in a healthy 50kg female S who was a heavy cigarette smoker. Knowledge of the pharmacokinetic properties of such drugs does not solve all problems regarding their clinical use, but the safety and effectiveness of antianxiety drug treatment can probably be enhanced by using pharmacokinetic considerations to guide therapy. 5 references. (Journal abstract modified)

229448 Goldstein, Michael J.; Rodnick, Eliot H.; Evans, Jerome R.; May, Phillip R. A. Department of Psychology, University of California, Los Angeles, CA 90024 **Long-acting phenothiazine and social therapy in the community treatment of acute schizophrenics.** Psychopharmacology Bulletin. 11(4):37-38, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, a study of the effectiveness of long-acting phenothiazine and social therapy in the community with acute schizophrenics was reported. Four groups of Ss were compared: those assigned to high-dose combined with family therapy; high-dose, no family therapy; low dose, no family therapy; and low dose combined with family therapy. Results suggest that young acute schizophrenics can be successfully maintained in the community with an aggressive aftercare program. Selection of dose level of long-acting phenothiazines is dependent on the psychosocial therapeutic resources available. Where family oriented crisis therapy is available, a relatively low dose of fluphenazine enanthate can be used to maintain Ss in partial remission in their communities. 2 references. (Journal abstract modified)

229556 Dotti, Andrea. Universita degli Studi di Roma, Istituto di Psichiatria, Rome **/Outpatient therapy with fluphenazine decanoate in schizophrenic patients./** La terapia ambulatoriale con decanoato di flufenazina in pazienti schizofrenici. Rivista di Psichiatria (Roma). 10(1):79-83, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, outpatient therapy with fluphenazine in schizophrenic patients was discussed. The Ss were between 18-40 years of age, and tended to have acute relapses with periods of relative well-being. A preliminary study indicated the relative utility of fluphenazine decanoate for treating acute and chronic psychoses with respect to treatment per os. A further study compared the results of administering an effective neuroleptic orally with those of intramuscular administration of a long-acting neuroleptic. Methodological problems involved in the second experiment were discussed.

229761 Kawajiri, Toru; Eto, Jun; Ishida, Tatsuo; Amamoto, Hiroshi. Dept. of Psychiatry, Seifukai Hikarigaoka Hospital, Japan **Influence of psychotropic drugs on chronic schizophrenic syndromes -- with special emphasis on the change in clinical process with a relatively high dosage of spiroperidol.** Medical Consultation & New Remedies (Tokyo). 12(3):681-689, 1975.

The effects of large doses of spiroperidol (SP) on chronic schizophrenia were studied in a comparative experiment in which 20 patients with schizophrenic history of more than 3 years were treated with SP (6-15 mg/day), promethazine (PR; 75-100 mg/day), and levomepromazine (100-300 mg/day) or chlorpromazine (150-400 mg/day) for 5 to 34 weeks. Ten patients showed remarkable improvement in their symptoms; six showed remarkable improvement within a certain period and remained the same thereafter; and four were unchanged. Sixteen patients lost their hallucinations and delusions through this treatment, and in the four other patients these symptoms decreased. Ten patients began to become aware of their illness and to acquire self-insight. No side-effects were observed. 11 references.

230780 Jain, R. C.; Ananth, J. V.; Lehmann, H. E.; Ban, T. A. Queen Street Mental Health Center, Toronto, Canada **A comparative study with pipothiazine palmitate and fluphenazine enanthate in the treatment of schizophrenic patients.** Current Therapeutic Research. 18(4):585-589, 1975.

A comparative, double-blind, clinical study with pipothiazine palmitate and fluphenazine enanthate was conducted in 30 chronically hospitalized schizophrenic patients. Both treatment groups showed statistically significant improvement in the total scores. It was noted, however, that more patients were discontinued prior to termination of the clinical trial for the pipothiazine palmitate group than for the fluphenazine enanthate group. Numerous adverse effects were recorded with both drugs. The most frequently occurring adverse effects were tremor and weight loss in the pipothiazine palmitate group and tremor and insomnia in the fluphenazine enanthate group. It is suggested that pipothiazine palmitate and fluphenazine enanthate are equally effective as psychotropic drugs in the maintenance treatment of chronic schizophrenic patients. (Author abstract modified)

230812 Ban, Thomas A. Division of Psychopharmacology, McGill University, Montreal, Quebec **Nicotinic acid in the treatment of schizophrenias: practical and theoretical considerations.** Neuropsychobiology (Basel). 1(3):133-145, 1975.

At the Atlantic Provinces Psychiatric Association Convention, held in St. John's, Newfoundland, in September 1973, practical and theoretical considerations on the use of nicotinic acid in the treatment of schizopphrenia were discussed. The literature on nicotinic acid in the treatment of schizophrenia was reviewed, and the results of the Canadian collaborative study were presented. The data indicate that nicotinic acid has no therapeutic effect on schizophrenia. 51 references. (Author abstract modified)

230823 Gerlach, Jes; Luhdorf, Kurt. Sct. Hans Hospital, Department E, DK-4000 Roskilde, Denmark **The effect of L-dopa on young patients with simple schizophrnia, treated with neuroleptic drugs: a double-blind cross-over trial with Madopar and placebo.** Psychopharmacologia (Berlin). 44(1):105-110, 1975.

The effects of L-Dopa on young patients with simple schizophrenia treated with neuroleptic drugs were examined. Thirteen out of 18 young outpatients with simple schizophrenia under neuroleptic treatment completed a double-blind cross-over trial with Madopar (L-dopa in combination with benserazid, a peripheral decarboxylas inhibitor) and placebo. L-dopa was effective against emotional withdrawal, blunted affect, tendency to isolation and apathy, without inducing or aggravating productive, accessory symptoms. The activity score, according to the specific activity withdrawal scale, was significantly increased, whereas the total BPRS score (Brief Psychiatric Rating Scale) was slightly, but significantly reduced. In cases where L-dopa had to be limited to 600 and 300mg daily, a tendency to anxiety, distortion of thinking, and a sense of unreality were observed, depending on the dose of L-dopa. In no case were gastrointestinal, cardiovascular or neurological side-effects observed. 31 references. (Author abstract modified)

230839 Brambilla, F.; Guerrini, A.; Guastalla, A.; Rovere, C.; Riggi, F. Ospedale Psichiatrico Paolo Pini, Via Ippocrate 45, Milano Affiori, Italy **Neuroendocrine effects of haloperidol therapy in chronic schizophrenia.** Psychopharmacologia (Berlin). 44(1):17-22, 1975.

The neuroendocrine effects of haloperidol therapy were examined in 62 male chronic schizophrenic patients, aged 16-62 years. The duration of the disease varied between 2 and 29 years. The patients were divided into 48 hebephrenics with onset of the disease at puberty, or immediately after puberty, and 14 paranoids with onset of the disease in adulthood. They received 6 mg of haloperidol, for 30 days, up to a total dose of 180 mg. The basic hormonal values revealed decreased secretion of total gonadotropins, follicle stimulating hormone (FSH) luteinizing hormone (LH), adrenocorticotrophic hormone (ACTH) and testosterone, and increased insulin secretion. The haloperidol therapy seemed to stimulate the secretion of FSH, LH, total gonadotropins, ACTH and testosterone, up to normal or low normal levels. No modifications were observed in the other hormonal variables. 36 references. (Author abstract modified)

230907 Master, Roshen S.; Kajaria, S. M.; Raheja, Sheila. B. J. Medical College, Poona, India **A controlled evaluation of "lorazepam" and diazepam in anxiety neurosis.** Indian Journal of Psychiatry (Madurai). 16(1):42-47, 1974.

The efficacy and tolerance of lorazepam vs diazepam in the treatment of anxiety neurosis were studied in a double-blind paradigm. Anxiety was measured by Hamilton's scale on a pretest/posttest basis and various serum metabolites were measured before and after treatment. After 2 weeks, both lorazepam and diazepam evidenced satisfactory effects. The incidence of side-effects was low with both drugs. It is concluded that lorazepam and diazepam are effective anxiolytics, but that a clinically satisfactory response occurs earlier with lorazepam. 5 references. (Author abstract modified)

231034 Pecknold, J. C.; Ban, T. A.; Lehmann, H. E.; Climan, M. Department of Psychiatry, McGill University, Montreal, Quebec **Clomacran in the treatment of schizophrenic patients: a comparison of two assessment methods.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(4):299-303, 1975.

At the Tenth Annual Meeting of the Canadian Society of Clinical Pharmacology, and Chemotherapy, held in Montreal in September 1974, it was reported that in an uncontrolled clinical trial, clomacran, the chlorpromazine analogue of the acridane series, was found to be therapeutically effective in the treatment of newly admitted schizophrenic patients. There was essentially no difference in ability of the two assessment

instruments, the Brief Psychiatric Rating Scale (BPRS) and Psychopathological Assessment Form (PAF), to detect therapeutic changes. On the other hand, the PAF, a 123 item scale, was found to be more sensitive for the description of a schizophrenic patient population than the BPRS, an 18 item scale. 4 references. (Author abstract)

231037 Chouinard, G.; Annable, L.; Melancon, J.; Chabot, M. St. Jean de Dieu Hospital, Montreal-Gamelin, Quebec, Canada **Chlorpromazine-induced electrocardiogram abnormalities.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(4):327-331, 1975.

The electrocardiographic abnormalities in patients receiving only chlorpromazine were evaluated and the roles of sex, age and length of illness in these abnormalities were assessed. Schizophrenic patients (48 male and 48 female patients) satisfying study criteria were selected for inclusion and changed from their old medication to a fixed dose of 125mg chlorpromazine daily. This uniformization period lasted 2 weeks, during which the electrocardiograms were taken after an overnight fast. Five patients were excluded because their electrocardiographic changes revealed the possibility of a organic heart disease. The electrocardiograms were found to be normal for 65.9% of the patients and abnormal for 34.1% Eleven percent of the patients were classified as demonstrating Grade I repolarization abnormalities, 14.3% of patients as Grade II, and 8.8% as Grade III. Chi-square tests revealed no significant differences between sexes, age groups or lengths of illness with respect to normality and grade of abnormality. 15 references. (Author abstract)

231277 Siris, Samuel G.; Docherty, John P.; van Kammen, Daniel P. NIH Clinical Center, Room 4N214, Bethesda, MD 20014 **The use of antidepressant drugs in schizophrenia.** Bethesda, MD, NIMH, 1975. 11 p.

Literature on the use of monoamine oxidase (MAO) inhibitors and tricyclic antidepressants in schizophrenia is reviewed, and new recommendations for clinical use of the agents are given on the basis of reported studies. Reports in which MAO inhibitors and tricyclic antidepressants are used alone are analyzed separately from those in which the drug is used in conjunction with a neuroleptic agent. Uncontrolled studies are clearly distinguished from double-blind controlled studies which are given more weight in the conclusions. From these data, it is concluded that: 1) it is not warranted to use antidepressants alone in schizophrenic patients except for a specially designated pseudoneurotic subgroup; 2) combined use of a neuroleptic and antidepressant is indicated only when signs and symptoms of depression other than anergia are present in a nonagitated patient and have not responded to neuroleptic medication; 3) paranoid symptomatology is not a contraindication to antidepressant medication; and 4) antidepressants must be used cautiously in young male schizophrenics with a history of psychiatric or behavioral disorder dating to childhood. 107 references. (Author abstract modified)

231367 Franchini, C. L.; Ferutta, A. M.; Rosina, P. L.; Arcioli, I.; Colonna, F. I Ospedale Psichiatrico Provinciale di Novara, Novara, Italy **/The problem of chronic schizophrenia: treatment with depot flupenthixol, a long-acting neuroleptic./** Il problema della schizofrenia cronica. Proposta di trattamento con flupentixol depot: neurolettico ad effetto prolugato. Neuropsichiatrica (Genova). 3(1-2):113-125, 1974.

Depot flupenthixol was used to treat 13 cases of chronic schizophrenia (10 paranoid schizophrenics, one simple schizophrenic and two hebephrenic schizophrenics). Good results were obtained with two paranoid schizophrenics, moderate results with two, null results with two, and four became worse. Good results were obtained with the simple schizophrenic; optimal results with one hebephrenic; and null results were found with the other. Side-effects such as insomnia, loss of appetite, hypotension, and psychomotor exitation were mild in all cases. After 10 months of treatment, three patients were discharged. 13 references.

231609 Burnett, Gordon B.; Little, Stephen R. C. J.; Graham, Norman; Forrest, Alistair D. Dept. of Psychiatry, Baylor College of Medicine, Texas Medical Center, 1200 Moursund Ave., Houston, TX 77025 **The assessment of thiothixene in chronic schizophrenia: a double-blind controlled trial.** Diseases of the Nervous System. 36(11):625-629, 1975.

The results of a double-blind controlled trial of the tranquilizer thiothixine (Navane) against chlorpromazine in 24 chronic schizophrenics in the Royal Edinburgh Hospital in Scotland are presented. Additionally, a limited experiment in withdrawal of routine tranquilizers in these patients was carried out prior to the trial. Changes in manifest psychosis and social disability were assessed by the Lorr scale and the Nurses' Observation Scale for Inpatient Evaluation (both given in an appendix) at suitable intervals. The results indicate that thiothixine conferred no advantage over chlorpromazine in symptom relief or social improvement. Serial measures showed no significant changes in these patients as a group when on active drugs as opposed to placebo, or with the course of time. Of the patients, 12.5% relapsed during the placebo period: these patients were younger than the nonrelapsers and had received larger daily doses of phenothiazines prior to the trial. 20 references. (Author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

225718 Prien, Robert F.; Caffey, Eugene, M.; Klett, C. James. Central Neuropsychiatric Research Lab, Veterans Administration Hospital, Perry Point, MD 21902 **Factors associated with treatment success in lithium carbonate prophylaxis: report of the Veterans Administration and National Institute of Mental Health Collaborative Study Group.** Archives of General Psychiatry. 31(2):189-192, 1974.

A multihospital collaborative study evaluating prophylactic lithium carbonate therapy in 205 patients with bipolar manic-depressive illness is presented. Poor lithium carbonate response factors were: 1) recent history of frequent affective episodes requiring hospitalization, and 2) previous failure of lithium carbonate treatment. Results suggest that lithium carbonate response may be related to the presence of schizoaffective illness and a family history of bipolar affective illness, but the small numbers of patients in these groups limit interpretation. Most failures on lithium carbonate therapy were found to occur during the first year. Ability to remain on the maintenance schedule with no episodes for a year is considered the most potent predictor of ultimate prophylactic success. Implications in these findings for the clinician's use in selecting patients for prophylactic treatment are discussed. 22 references. (Author abstract)

226411 Jacobsson, L.; Glitterstam, K.; Palm, U. Dept. of Psychiatry, Umea University, S-901 85 Umea, Sweden **Objective assessment of anticholinergic side effects of tricyclic antidepressants.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:47-53, 1974.

A double-blind crossover comparison between imipramine and imipramine-N-oxide was performed with respect to the an-

ticholinergic side-effects on salivation and accommodation. Fifteen healthy male volunteers were given 25 mg. of each drug three times daily for 3 days, after which time salivation and accommodation were measured. There was significantly less impairment of salivation found after imipramine-N-oxide medication than after imipramine, while no significant difference was found regarding accommodation. It is concluded that the differences found between the two drugs favor imipramine-N-oxide. 14 references. (Author abstract modified)

226612 Hofmann, G.; Grunberger, J.; Konig, P.; Presslich, O.; Wolf, R. Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1097, Wien, Austria **/The long-term lithium treatment of affective disorders. long-term effects and side-effects./** Die mehrjahrige Lithiumtherapie affektiver Storungen: Langzeiteffekte und Begleiterscheinungen. Psychiatria Clinica (Basel). 7(3):129-148, 1974.

Some questions of the long-term lithium treatment of affective disorders are discussed based on a statistical analysis of 140 patients. The overall results are considered not to differ from those published elsewhere. After 4 years of treatment the number of symptom free female cases is felt to be increasing beyond 50%, while another 25% show only subclinical phases. The 4 year results in men are not favorable, and in the fourth to sixth year they are slightly worse. The difference in therapeutic effects between recurrent unipolar and circular depression is apparent only in men. The prophylaxis of relapses of mania is less successful than that of depressions in both sexes. Changes in the course of the illness, in the general condition of the patient and in the endogenous rhythmicity occur mainly in the beginning of lithium therapy, and are probably slightly more frequent than those associated with other psychotropic drugs. The incidence of side effects is considered somewhat lower after several years of lithium treatment than in the early stages. A form of an organic psychosyndrome appearing during long-term lithium therapy is discussed. 50 references. (Author abstract)

226777 Baer, R. Univ.-Nervenklinik mit Poliklinik, 852 Erlangen, Schwabachanlage 10, Germany **/Psychovegetative disorders in cases of cyclothymic depression./** Psychovegetative Storungen bei zyklothymer Depression. Medizinische Welt (Stuttgart). 25(8):311-313, 1974.

The psychovegetative disorders in cases of cyclothymic depression are described. The symptoms include disturbance of sleep, lack of appetite, diminished libido. Malfunctions of individual organs include obstipation, hyperperspiration, dry throat due to therapy, dizziness, and tachicardia with measurable irregularity of blood pressure amplitude and low mydriasis. In cases of retarded depressions with narrow symptom spectrum, stimulationg thymoleptics are recommended. In agitated depressions or bipolar processes of depression, affect-inhibiting psychotropics are recommended, or a combination of thymoleptics with mild neuroleptics. Application of thymoleptics (late in the day) are cautioned against particularly in cases of depressions with unstable day rhythm. (Author abstract modified)

226778 Freyberger, H.; Leutner, V. 2000 Hamburg, Martinistr. 52, Germany **/Pharmacotherapy in psychovegetative disorders./** Pharmakotherapie bei psychovegetativen Storungen. Medizinische Welt (Stuttgart). 25(8):313-316, 1974.

An overview on effectivity, specificity, and utility in practical therapy of commercial psychotropics relevant for psychovegetative disorders is given. Drugs are classified under vegetative therapeutics (Bellergal and other brands), neuroleptics, and tranquillizers and broad range psychosomatics. Areas of therapeutical indication are discussed and six different possible effects of therapy are identified: anxiolytic effect, sedation effect and facilitation of sleep, muscle relaxation effect, vegetatively regulating effect, antidepressant effect, and pain killer effect. In conclusion, four main strategies of therapy are identified: day tranquillizers for anxiolytic effect without sedation, standard tranquillizers for 24 hours and over effectivity, broad range tranquillizers for stronger and immediate effectivity, and broad range psychosomatics for even stronger and more varied effects.

226794 Kline, Nathan S. no address **/The causes and treatment of depression./** From sad to glad. New York, Putnam, 1975. $7.95.

Depression, new drugs used to treat it, and its susceptibility to treatment are discussed. Depression is considered as a transient biochemical disorder; clinical material is included to illustrate associated symptoms. The use of antidepressant drugs, as opposed to psychoanalytic therapy, is advocated in the treatment of depression. The need to demythologize depression is emphasized.

226898 Priest, Robert G.; Netter, Petra. St. Mary's Hospital Medical School, University of London, Harrow Road, London W9 3RL **Hostility, somatic symptoms and recovery with antidepressants.** International Pharmacopsychiatry (Basel). 10(3):137-141, 1975.

In a study of hostility, somatic symptoms and recovery with antidepressants, patients were treated with protriptyline or nortriptyline (double-blind). They were assessed on the Zung Depression Scale and on the Hostility and Direction of Hostility Questionnaire (HDHQ). A good response was heralded by low ratings on criticism of self and others, and on projected (paranoid) hostility. The outcome was better with initial low scores on depressive symptoms, particularly unworthiness, restlessness and constipation. Associations between initial and later side-effects are noted: initial loss of interest was associated with later drowsiness, lack of clear mind with blurred vision, loss of libido with constipation, and ideas of suicide with dry mouth. 8 references. (Author abstract)

226899 Sim, Myre; Reid, David; Pallett, Joyce; Gordon, Edward. Department of Psychological Medicine, United Birmingham Hospitals, Birmingham, England **The Hamilton Rating Scale. An assessment based on a dothiepin ('Prothiaden') versus imipramine ('Tofranil') clinical trial.** International Pharmacopsychiatry (Basel). 10(3):142-148, 1975.

The Hamilton Rating Scale for Depression is compared with a system of psychiatric assessment and recording designed by M. Sim. In a clinical comparison of dothiepin (Prothiaden) and imipramine (Tofranil), it was found that there was closer agreement with the full assessment of the Sim method than with the single diagnostic area for depression. This suggests that the Hamilton Scale for depression is more general than specific in its application. 6 references. (Author abstract modified)

226915 Gaillard, Jean-Michel; Constantinidis, Jean; Tissot, Rene. Clinique psychiatrique universitaire de Bel-Air, CH-1225 Chene-Bourg, Switzerland **Effect of peripheral decarboxylase inhibition on HVA and 5HIAA in cerebrospinal fluid of depressed patients.** Neuropsychobiology (Basel). 1(1):26-31, 1975.

The effects of benserazide on the level of homovanillic acid and 5-hydroxyindoleacetic acid in cerebral spinal fluid (CSI) were investigated in 1 manic and 11 depressed patients. Benserazide induced no change on both metabolites. This negative result supports the view that monoamine metabolites in CSF, in the absence of loading with an exogenous precursor, originate mostly from brain parenchyma, without significant contribution of the metabolism in capillary walls. 19 references. (Author abstract)

227205 Eccleston, D. Brain Metabolism Unit, Edinburgh, Scotland **Modern views on diagnosis and classification of depressions: II. United Kingdom.** Journal of International Medical Research (Northampton). 3(Suppl. 3):3-6, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the catecholamine hypothesis and its variants for the cause of affective disorders were discussed. It was stated that the biological basis in man for the hypothesis is negligible. It was also noted that drugs which are useful in mania, a supposed polar opposite of depression, are if anything more potent in the blockade of central dopaminergic receptors rather than noradrenergic, and that recent reports reveal the possibility that increased central cholinergic activity also produces a transient defervescence of manic symptoms. The possibility was explored that the dopamine system in man is the background driving force, important to him not only with his basic biological drives but also to propel him forward into his social contracts and integration. Mood was described as a partially dependent variable which can and does become clinically dissociated from the psychomotor phenomena. A closer examination of the clinical states of depression, mania and Parkinsonisn was recommended. 10 references. (Author abstract modified)

227214 Mahapatra, S. B. Department of Psychiatry, University of Leeds, England **Short term effects of viloxazine (Vivalan) compared with placebo in depression: a double-blind study.** Journal of International Medical Research (Northampton). 3(Suppl. 3):70-74, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study was reported in which 36 hospitalized depressive patients entered a double-blind comparative study of viloxazine and placebo. Twenty one patients took viloxazine while 15 took placebo. The depressive symptoms were assessed by using the Hamilton Rating Scale for Depression before and on the third and seventh day of treatment. There were no significant differences between the viloxazine and placebo groups on days 3 or 7. However, when the scores on the items of depressed mood, guilt and suicidal tendencies, were analyzed separately there emerged a statistically significant difference between active and placebo drugs on day 3 with viloxazine producing the lower score. These results were seen with patients receiving viloxazine, irrespective of whether they had previously been given antidepressant therapy. Side-effects were reported by a high proportion of patients of both groups, but were more severe in patients on viloxazine. 4 references. (Author abstract modified)

227215 Ekdawi, M. Y. Coulsdon, England **Viloxazine (Vivalan) comparison with imipramine.** Journal of International Medical Research (Northampton). 3(Suppl. 3):75-78, 1975.

At the International Vivalan Symposium, held in London in November 1974, a double-blind study to compare the relative efficiency of viloxazine, a new nontricyclic antidepressant, and imipramine in depressed patients was reported. The two drugs were found to be equally effective in 29 patients treated with viloxazine and 30 with imipramine over a period of 6 weeks, using the Hamilton Rating Scale for measuring response. Viloxazine, however, appeared to produce a more rapid response; it caused fewer and less persistent side-effects and significantly lower bodyweight gain than imipramine. 6 references. (Author abstract modified)

227216 Pichot, P.; Guelfi, J.; Dreyfus, J. F. Paris, France **A controlled multicentre therapeutic trial of viloxazine (Vivalan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):80-86, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the effects of viloxazine (Vivalan) and imipramine in depressive states that were of neither schizophrenic nor organic origin were compared. The results after full statistical analysis indicate that the action of viloxazine in depression was at least equivalent to imipramine in the doses used and that, overall, viloxazine produced fewer side-effects, although digestive symptoms and headache occurred more frequently. (Author abstract modified)

227217 Brion, S. Centre Hospitalier de Versailles, France **Open studies with viloxazine (Vivalan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):87-91, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study was reported in which 112 patients with a variety of types of depressive illness were treated in an open trial with viloxazine at doses of 200-300mg/day. Fifty percent of the total group were either returned to normal or markedly improved, and a further 12.5% showed lesser improvements. Thirty nine patients complained of possible side-effects, but in only 14 were these severe enough to lead to withdrawal of the agent. The predominant side-effects were gastrointestinal in origin, but were generally mild and transient and did not interfere with treatment. No cardiac effects were noted, and the drug was safely administered to four epileptic patients with depression. An increase in anxiety was noted in four patients, leading to withdrawal in two patients; two patients withdrew from treatment due to manic switch. It was suggested that these effects can be prevented by coadministration of a tranquillizing drug to patients with a high level of anxiety or with manic-depressive psychosis. It was concluded that viloxazine possesses good antidepressive properties without troublesome side-effects, at doses of 200-300mg/day. The preliminary results from 23 patients in a further open trial indicate that the drug also possesses good antidepressive activity at a dose of 150mg/day. (Author abstract modified)

227218 Guz, I. Sao Paulo, Brazil **Open studies with viloxazine (Vicilan).** Journal of International Medical Research (Northampton). 3(Suppl. 3):92-94, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study of the use of viloxazine in the treatment of depression was reported. The majority of subjects responded during the second week. By the third week 28 patients showed marked improvement. In some patients it was possible to compare the therapeutic effects of viloxazine with those of previously administered drugs currently in use for the treatment of depression. The results, as a rule, were very similar to those obtained with imipramine but the initial response time seemed to be shorter with viloxazine than with other drugs. It was concluded that viloxazine is a novel chemical substance with antidepressant activity. It is active in all forms of depression and neurotic depressions: it was less effective in involutional and atypical depressions.

227220 Ichimaru, I. no address **Additional studies -- Japan.** Journal of International Medical Research (Northampton). 3(Suppl. 3):97, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the antidepressant activity and side-effects of viloxazine prior to carrying out a controlled study were tested. Nine outpatients received 120-240mg/day of viloxazine and global ratings were assessed initially and at weekly intervals for 4 weeks. At the completion of the trial, five out of nine patients showed improvement of symptoms; three were worse and one had no change. The side-effects were mainly gastrointestinal. In an effort to control the gastrointestinal side-effects, enteric coated viloxazine tablets were given to 14 patients and in this trial, by week 4, 11 showed improvement, with three having no change. No side-effects were reported. Clinical investigation of blood counts, blood urea nitrogen, electrocardiogram, and liver function were carried out at the third week, and results were all within normal limits. It was confirmed that viloxazine possesses antidepressant activity and gastrointestinal side-effects can be prevented by the use of enteric coated tablets.

227221 Lopez Zanon, A. Madrid, Spain **Additional studies -- Spain.** Journal of International Medical Research (Northampton). 3(Suppl. 3):98, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study was reported in which 100 depressed patients entered a double-blind, between patient study of viloxazine hydrochloride 200mg/day (expressed as base) or imipramine hydrochloride 100mg/day (expressed as salt), each for 28 days. Of the viloxazine treated patients, 64% showed a marked improvement, whereas only 36% of the imipramine group responded in this way. However, when moderate improvement was added to these figures, the percentages response rate for viloxazine became 74% and for imipramine 60%. A high proportion (about 88%) of the marked improvements was maintained on both drugs and of the moderate improvements on imipramine, 75% were maintained while none of those on viloxazine were. There was a higher incidence of possible side-effects on imipramine (18%) than on viloxazine (6%) but most of the problems with imipramine were associated with a failure of the drug to control anxiety. It was concluded that viloxazine is an effective antidepressant with an overall response rate similar to that of imipramine, but that there are more marked improvements with viloxazine which may be due to its having a faster onset of action.

227222 Ouri, P. Mikkeli-Moisio, Finland **Additional studies -- Finland.** Journal of International Medical Research (Northampton). 3(Suppl. 3):99, 1975.

At the International Vivalan Symposium, held in London in November 1974, a study was reported in which 13 depressed, hospitalized patients were given daily doses of either 200 or 300mg viloxazine hydrochloride (Vicilan) in an open study for periods of up to 6 weeks. As early as the third day of treatment, a statistically highly significant reduction in Hamilton Rating Scores was seen, and this fall continued throughout the study. Only one patient showed no response to the drug. The medication was generally well tolerated, the only side-effects seen (nausea and vertigo) being transient or controllable on reduction of dose. No patient had to be withdrawn from treatment because of side-effects, and all laboratory hematological tests remained normal during the study. It was concluded that viloxazine is an effective, rapid acting antidepressant with a high response rate and which merits a controlled evaluation.

227224 Wheatley, D. P. General Practitioner Research Group, Twickenham, England **Viloxazine (Vivalan) -- a new antidepressant.** Journal of International Medical Research (Northampton). 3(Suppl. 3):105-110, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which four dose levels of viloxazine (Vivalan) (120, 200, 240 and 300mg daily) were compared in 77 depressed patients, treated for 4 weeks. Similar results were recorded with all four schedules, there being no statistically significant differences on the three measures, physicians rating scales, patient self-assessment or global ratings, at any period of the trial. Results were similar to those recorded with tricyclic antidepressants. However, an important advantage for viloxazine was apparent in the fact that there was only one case of drowsiness at 3 days and only three cases of dry mouth. On the other hand, on the two higher doses, nausea occurred fairly frequently and necessitated omission of treatment in a number of cases. It was concluded that the optimum dose for treating ambulatory patients at home is 200mg daily. (Author abstract modified)

227225 Bayliss, P. F. C. Clinical Research Department, ICI Limited, Macclesfield, England **Multicentre studies in general practice.** Journal of International Medical Research (Northampton). 3(Suppl. 3):111-114, 1975.

At the International Vivalan Symposium, held in London 1974, a study was reported in which 48 mild to moderate depressives were treated by six general practitioners with a chemically novel antidepressant, Vivalan, (viloxazine hydrochloride, ICI 58,834). Twenty five patients took 150mg/day in three divided doses, and 23 took 200mg/day in two divided doses, each for 21 days. The severity of both the depressive syjptoms and the anxiety symptoms showed a statistically highly significant reduction over the duration of the study. There was no difference between the efficacy of the two dose levels. Viloxazine was generally well tolerated and there was no difference between the two dose levels as far as side-effects or withdrawals were concerned. The usual sedative and anticholinergic side-effects of the tricyclic antidepressants were virtually absent. The only side-effect seen was a transient upper gastrointestinal disturbance. It was commoner at the high dose but not significantly so. It was concluded that viloxazine hydrochloride is an effective antidepressant in this type of patient and produced little or no sedative or anticholinergic side-effects. Either 150mg/day or 200 mg/day was recommended as a reasonable dose to use in general practice. 2 references. (Author abstract)

227226 Murphy, J. E. Clinical Research International, Northampton, England **Viloxazine (Vivalan) -- general practitioner group studies.** Journal of International Medical Research (Northampton). 3(Suppl. 3):115-119, 1975.

At the International Vivalan Symposium, held in London in Novemeber 1974, a study was reported in which 123 patients with mild to moderate depressive illness were entered into a double-blind between patient study of viloxazine hydrochloride (150mg/day) and imipramine hydrochloride (75mg/day) by nine general practitioners. Sixty two took viloxazine and 61 took imipramine. Both drugs produced a statistically highly significant improvement in both the depressive and anxiety symptoms over the period of the study; an effect was seen as early as the seventh day of treatment. Viloxazine produced fewer side-effects than imipramine, in particular significantly less drowsiness and dry mouth. The only side-effect seen with Niloxazine was an upper gastrointestinal disturbance with nausea and occasional vomiting, but this was transient. It was

concluded that viloxazine hydrochloride is an effective antidepressant in mild to moderate cases of depression in general practice and has the advantage of fewer side-effects than imipramine. The absence of sedation with viloxazine is of particular value in the treatment of ambulant patients. 3 references. (Author abstract modified)

227413 Cade, J. F. J. Psychiatric Hospital, Oak Street, Royal Park, Victoria, 3052, Australia **Lithium -- when, why and how?** Medical Journal of Australia (Sydney). 1(22):684-686, 1975.

A general discussion on the use of lithium in manic, manic-depressive, schizoaffective, and unipolar depressive illness, and in cyclothymia is presented. Topics covered include the decision to use lithium and its management, dosage schedules, base or steady state blood levels, side-effects and toxic effects, frequency of blood level determination, thyroid function, and diabetes. It is noted that the lithium patient's sodium intake must be adequate to guard against the precipitation of lithium toxicity. 2 references.

227572 Mikkelsen, Edwin J.; Rosenbaum, Alan H. Dept. of Psychiatry, Massachusetts Mental Health Center, Boston, MA 02115 **Amitriptyline-perphenazine overdose producing delayed hypomania in manic-depressive illness.** American Journal of Psychiatry. 132(8):870-871, 1975.

A case history is given of a 26-year-old woman who became hypomanic after awakening from a semicomatose state induced by an overdose of amitriptyline-perphenazine (Triavil). She had been depressed and had a strong family history of manic-depressive illness. The case is reported to support previous evidence that dopamine is a mediator for mania. 5 references. (Journal abstract modified)

227746 Latimer, P. R.; Braden, D. H. Queen's University, Kingston, Ontario **Roussy-Levy syndrome with psychosis.** Canadian Psychiatric Association Journal (Ottawa). 20(4):287-289, 1975.

In the case of a 39-year-old woman with Roussy-Levy syndrome (hereditary ataxia with muscular atrophy) and psychosis is reported. The patient was suspicious of staff and demonstrated olfactory hallucinations and incongruous affect throughout the initial 9 days of hospitalization. It was felt that this represented a paranoid psychosis of rapid onset, which responded promptly to thioridazine. Recovery was apparently complete. Five months after discharge, neither the family nor the personal physician noted any recurrence of the acute psychotic symptoms; the S continues to take thioridazine. There was little evidence to suggest that the psychiatric symptoms resulted from a progression of her degenerative neurological disease. 3 references. (Author abstract modified)

227768 Meurice, Emile Institut Psychiatrique Provincial, B-6688, Lierneux, Belgium **Ataraxic and antimanic effects of thioxanthenes.** Acta Psychiatrica Belgica (Bruxelles). 74(5):516-519, 1974.

At the first joint meeting of the Scandinavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the ataraxic and antimanic effects of thioxanthenes were discussed. Clopentixol was suggested as the drug of choice in treatment of agitated states; the ratio of antimanic action to hypotension and excitatory motor side-effects is high, while the rate of antimanic effect to hypogenic effect is low, as compared to other neuroleptics. It is noted that the aim of treatment is not the reduction of symptoms at any cost but restoration of the patient's ability to interact socially at his best level. From that standpoint, it was concluded that the ratio of therapeutic effect/side-effect is especially good for the thioxanthene derivatives.

227785 Post, Robert M.; Gerner, Robert H.; Carmen, John S.; Bunney, W. E., Jr. no address **A dopamine receptor stimulator in depression. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 24 p.

At the Annual American Psychiatric Association Convention, held at Anaheim, California, in May 1975, preliminary findings of the first clinical trial of piribedil (ET-495) in depressed patients were reported. Piribedil is a drug which specifically stimulates dopamine receptors. Of five depressed patients, all demonstrated some antidepressant effect; two patients had rather substantial antidepressant responses, one of whom had a rebound in depression upon drug withdrawal. Two patients currently involved in their clinical trial showed preliminary antidepressant effects. One manic patient treated with low doses appeared to have an antimanic response to piribedil and one schizoaffective patient remained in his acute illness while treated with relatively high doses of the agent. Findings suggest that the drug may possess some antidepressant potential, but that it should be used cautiously, as it may be associated with the activation of mania in highly predisposed individuals. Results substantiate data suggesting that dopamine may be critical neuroregulator in the cyclic mood disorders.

227826 Itil, T. M.; Patterson, C. D.; Polvan, N.; Bigelow, A.; Bergey, B. Division of Biological Psychiatry, Dept. of Psychiatry, New York Medical College, New York, NY **Clinical and CNS effects of oral and i.v. thyrotropin-releasing hormone in depressed patients.** Diseases of the Nervous System. 36(9):529-536, 1975.

In a study of the effects of thyrotropin releasing hormone (TRH) administered to depressive patients, it was found that both oral and i.v. TRH produced systematic alterations in brain function as determined by scalp recorded computerized electroencephalograms (CEEG). The CEEG profiles of the oral and i.v. preparations were not only very similar to each other, but also resembled the profiles of stimulants such as d-amphetamine, isocarboxazid and methylphenidate. Thyroid stimulating hormone (TSH) plasma levels after TRH indicated that TRH is an active compound. Some antidepressant activity was seen but this effect was not consistent. In almost all patients, an increase of interest, desire and drive for work, food and sex was noted, particularly after i.v. TRH. It is suggested that this latter effect was responsible for the antidepressant activity of TRH in patients in whom depression may have been the result of an inhibition of instinctive functions. 20 references. (Author abstract modified)

228037 Flach, Frederic F.; Draghi, Suzanne C. no address **The nature and treatment of depression.** New York, John Wiley and Sons, 1975. 422 p. $19.75.

The etiology and treatment of depressive and manic illnesses are discussed. The biogenic amine hypothesis concerning genetic origins of depression is reviewed. The role of hatred or anger in the pathogensis of severe depression and evidence of the contribution of some environmental factors are considered. Other topics considered include: the psychology of depression in adults and children; the recognition of potential suicides; pharmacotherapy; the sleep of the depressed adult; childhood bereavement; social isolation; and the correlation of neurotransmitters with complex behavioral, cognitive, and emotion changes.

228217 Goswami, S. N. 6/3 Borla Co-op. Housing Society, Bombay 400 074 India **Lithium in psychiatry.** Maharashtra Medical Journal (Poona). 21(7):251-264, 1974.

A review of the use of lithium in psychiatry is presented. Lithium is indicated in mania, manic-depressive psychosis and recurrent depression. Its dosage is highly individualized and should be strictly guided by regular serum lithium estimations; a serum lithium concentration of 0.5to 1.7mEq/liter usually provides clinical control of affective disorders with minimal side-effects. Lithium therapy, unless considered essential, should be avoided in women of childbearing age. On a comparative basis, lithium has been shown to be a more useful psychotropic agent than chlorpromazine in the treatment of mania and manic-depressive psychosis. Combined use of lithium with chlorpromazine or other psychotropic agents has been shown to be useful in treating affective disorders. Slow release lithium carbonate preparations have been shown to produce fairly constant serum lithium following a morning dose, but further research is necessary in this area. 62 references.

228226 Takahashi, Ryo; Sakuma, Akira; Itoh, Kozo; Itoh, Hitoshi; Kurihara, Masanao; Saito, Masami; Watanabe, Masasuke. Dept. of Neuropsychiatry, Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852, Japan **Comparison of efficacy of lithium carbonate and chlorpromazine in mania: report of collaborative study group on treatment of mania in Japan.** Archives of General Psychiatry. 32(10):1310-1318, 1975.

A multi institutional cooperative study comparing lithium carbonate (LC) with chlorpromazine (CPZ) was conducted, using a double-blind controlled design in a series of 80 cases of endogenous manic psychosis, to evaluate the drugs' clinical utility and efficacy, characteristics of therapeutic effect, and side-effects. Dosages employed were consistently at an equipotent ratio of 4:1 (LC:CPZ). Physicians' overall ratings showed LC to be significantly superior to CPZ in efficacy for manic psychosis. Improvements of basic mood and of disturbance in speech and voice were prominent with LC. Onset of the therapeutic effect of LC was within 10 days of medication in 65% of the patients, significantly faster than with CPZ. Side-effects encountered with LC at dose levels not higher than 1800mg/day were milder and less frequent than those seen with CPZ. The results, which were obtained with Japanese patients, are compared with those of studies conducted in the U.S. 30 references. (Author abstract modified)

228327 Okuma, Teruo; Sunami, Yuzuru; Miyamoto, Keiichi. Department of Neuro-psychiatry, Tohoku University School of Medicine, Japan **A double-blind controlled comparison of clomipramine (anafranil) and imipramine on depression.** Clinical Psychiatry (Tokyo). 17(3):283-286, 1975.

The effects of clomipramine and imipramine on depression were studied in a double-blind experiment. Eighty three patients with endogenous depression were treated with either clomipramine or imipramine for 5 weeks. No significant difference between the two drugs was observed in their effects, side-effects and rapidity of action. The two drugs were moderately to extremely effective on 67% of the patients, and the effects appeared within 14 days after the beginning of treatment. The two drugs induced dry mouth in 45% of the patients, tremor in 35%, dizziness in 30%, and drowsiness in 25%. 5 references.

228334 Tamura, Atsuko. Department of Neuro-psychiatry, Tokyo Women's Medical College, Japan **Clinical experience in using sulpiride (FK-880) for depression.** Medical Consultation & New Remedies (Tokyo). 12(2):373-397, 1975.

The effect of sulpiride on depression was studied, based on a clinical administration of this drug for 1 week to 18 months with or without other psychotropic drugs to 51 outpatients with depression (Group A), six patients in a transient phase from mania to depression (group B), four patients with chronic manic illness (Group C), two patients with advanced manic illness and manic depression (Group D), and one patient with manic illness (Group E). The drug was effective in 30 patients in Group A, all in Group B, and three patients in Group C. This drug was effective on depression, anxiety, irritation, and tension. Side-effects were observed in 22 patients, including Parkinsonism, fatigue, drowsiness, dizziness, insomnia, restlessness, and akathisia. Since many patients were treated with other psychotropic drugs at the same time, definite effects and side-effects of sulpiride could not be determined. 34 references.

229236 Knauth, Percy. no address **The silver violin string.** MH -- Nat'l. Assn. of Mental Health. 59(3):15-16, 1975.

A recovered depressed patient traces the course of his improvement and describes the approach of a relapse when antidepressant medication was terminated. It is concluded that psychotherapy and medication are both elements in recovery and maintenance of emotional equilibrium.

229437 Perel, James M.; Hurwic, Maria J.; Kanzler, Maureen B. College of Physicians and Surgeons, Columbia University, New York, NY **Pharmacodynamics of imipramine in depressed patients.** Psychopharmacology Bulletin. 11(4):16-18, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 the pharmacodynamics of imipramine use in depressed patients were reported, based on tentative data obtained for one group of such patients, in which steady state plasma levels of antidepressants (imipramine and desmethylimipramine) varied from 95 to 1020ng/ml with a mean of 210 plus or minus 110ng/ml. These levels were obtained with chronic oral adminisration of 3.5mg/kg of imipramine per day in three divided doses. Most of the observed interindividual variablity in plasma levels was due to differences in rate of metabolism of the drug. An additional significant source of variablity was the volume of distribution. Two fold differences in this parameter were directly related to the fraction of unbound antidepressant in plasma. The distribution of plasma steady state levels of imipramine and desmethylimipramine was compared in 22 smoking and nonsmoking depressed Ss. Striking differences were found, with smokers having markedly lower levels, (160ng/ml), as compared with nonsmokers (190ng/ml). 13 references. (Journal abstract modified)

229443 Glassman, Alexander H.; Shostak, Michael; Kantor, Shepard J.; Perel, James M. Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY **Plasma levels of imipramine and clinical outcome.** Psychopharmacology Bulletin. 11(4):27-28, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 a study of the impact of varying plasma levels of tricyclic antidepressant drugs, such as imipramine (IMI), on clinical outsome in seriously depressed inpatients was reported. Ss were maintained drug free for a minimum of 1 week and were carefully evaluated for suitability. Those selected were given 3.5mg/kg/day of imipramine hydrochloride and plasma levels or both IMI and desmethylimipramine (DMI) were measured three times per week for 4 weeks. Findings indicate that among these serioulsy unipolar depressed, nondelusional patients, there was

a clear relationship between plasma level and drug response, and that a significant proportion of such patients given apparently adequate oral doses will not reach plasma levels necessary to obtain a therapeutic response. 9 references. (Journal abstract modified)

229449 Lipman, Ronald S.; Covi, Lino; Smith, Virginia K. Psychopharmacology Research Branch, NIMH, Rockville, MD 20852 **Prediction of response to drug and group psychotherapy in depressed outpatients.** Psychopharmacology Bulletin. 11(4):38-39, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, a predictive study of response to drug and group psychotherapy in the treatment of depression was reported. Chronically depressed women who continued to show mild to moderate depression following a 2 week placebo washout period were randomly assigned to either dynamically oriented group psychotherapy or to brief supportive contact and to one of three medications: imipramine, a tricyclic antidepressant, or placebo. After 1 week of treatment, group psychotherapy Ss improved more than the minimal contact Ss and placebo Ss on a number of mood scales, while diazepam Ss improved more on sleep difficulty measures and on friendliness, well-being, carefreeness, and activity. By 2 weeks, group psychotherapy advantages were lost. By 8 weeks, imipramine effects were stronger and more general. At 16 weeks, imipramine and group therapy patients generally showed more improvement than other Ss, but some diazepam patients on estrogen did quite well. Overall, the strongest predictors of outcome were initial level of distress and the main effect and interaction effects of medication. Group psychotherapy and its modifiers accounted for less than half of the explained variance by medication effects. 5 references. (Journal abstract modified)

229450 Weissman, Myrna M.; Prusoff, Brigitte A.; Klerman, Gerald L. Yale University School of Medicine, Department of Psychiatry, New Haven, CT 06520 **Drugs and psychotherapy in depression revisited: issues in the analysis of long-term trials.** Psychopharmacology Bulletin. 11(4):39-41, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974. A study of the long-term effects of multifactorial, multioutcome maintenance trials using both drugs and nonsomatic therapies was reported. Recovering depressed women were randomly assigned to 8 months of maintenance amitriptyline, placebo, or no pill with or without psychotherapy. Results demonstrate the feasibility, efficacy and safety of maintenance amitriptyline in depression, and that drugs and psychotherapy do not have harmful interactions. Evidence for a psychotherapy effect occurred, but its magnitude or consistency was not fully assessed. Overall, it appears that psychotherapy has an effect on enhancing social adjustment and that this effect may be dependent upon prior symptom reduction and sufficient time. Further research to specifically determine the place of psychotherapy in treating depression is needed. 5 references. (Journal abstract modified)

229642 Essman, W. B. Department of Psychology, CUNY, Queens College, Flushing, NY 11367 **Lithium.** Lancet (London). 2(7934):547, 1975.

Evidence to support the contention that the lithium/magnesium relationship, a factor cited in the pharmacological action of lithium, involves biogenic amines is reported. The effect of lithium salts on affective disorders and the suggested role of 5-hydroxytryptamine (5-HT) in the etiology, sequelae, and therapy of affective disorders indicate that magnesium may be a common key to both pharmacological action and neurochemical change. The suggestion that alkaline earth metal metabolism may be a fundamental defect in recurrent affective disorders appears more plausible when it is considered that a magnesium deficiency state affects brain Mg and 5-HT, and that lithium alters the deficiency in both the cation and the amine. 15 references.

229693 Evans, L. E. J.; Hunter, P.; Hall, R.; Johnston, Moira; Roy, V. Mathew. no address **A double-blind trial of intravenous thyrotrophin-releasing hormone in the treatment of reactive depression.** British Journal of Psychiatry (London). 127:227-230, 1975.

In a double-blind trial, 600mcgs of thyrotrophin releasing hormone (TRH) was compared with placebo given daily for 4 days to two groups of 10 patients. The subjects were patients suffering from reactive depression. Both TRH and placebo (saline) were given intravenously. It was found that i.v. TRH was no better than saline in the treatment of reactive depression. The improvement seen in both drug and saline groups was attributed to the time and attention given to the patients during the course of the trial. 11 references. (Author abstract modified)

229760 Noguchi, Takuro; Motomura, Hiroshi; Shima, Tadasu. Department of Psychiatry, Saitama Medical University, Japan **Clinical experience in using Maprotiline, a new anti-depressive medicine.** Medical Consultation & New Remedies (Tokyo). 12(3):671-679, 1975.

The effect of Maprotiline (CIBA-34,276-Ba) on depression was studied, based on an experiment in which 20 patients with various types of psychotic depression and 7 with neurotic depression were treated with this drug (25 mg/day) for 2 to 20 weeks. Findings indicate that Maprotiline was extremely effective in 7.4% of the patients, effective in 37%, slightly effective in 29.7%, and not effective in 25.9%. The overall effectivity rate was 74.1%. The effectivity rate of the patients excluding those with neurosis was 85.0%. Maprotiline was especially useful in treating endogenous depression, including manic-depression and involutional melancholia, but was not very effective in neurotic depression. Drug effects appeared within 2 to 4 weeks after the inception of treatment. Side-effects were observed in 25.9% of the patients, including fatigue, dry mouth, dizziness, bitter taste in the mouth and lisping. 6 references.

229827 Fischer, E.; Heller, B.; Nachon, M.; Spatz, H. Laboratorio de Psicofarmacologia y Neuropsiquiatria, Hospital Nacional Jose T. Borda, Barracas 375, Buenos Aires, Argentina **Therapy of depression by phenylalanine: preliminary note.** Arzneimittel-Forschung (Aulendorf). 25(1):132, 1975.

Treatment of endogenous depression with d,l-phenylalanine and d-phenylalanine is reported. Ss all had long-term endogenous depression, and all had been treated unsucessfully with imipramine like drugs and/or inhibitors of monoamineoxidase. Ss were given daily oral doses of 50mg or 100mg of either drug over a period of 15 days. Complete euthymia was obtained in 74% of the Ss between 1 and 13 days of treatment. Side-effects were minimal and in no case required termination of treatment. 13 references. (Author abstract modified)

230816 Shopsin, Baron; Janowsky, David; Davis, John; Gershon, Samuel. Department of Psychiatry, Neuropsychopharmacology Research Unit, New York University School of Medicine, New York, NY 10016 **Rebound phenomena in manic patients following physostigmine: preliminary observations.** Neuropsychobiology (Basel). 1(3):180-187, 1975.

A rebound phenomena in manic patients following physostigmine is described. Physostigmine was administered intravenously to three hospitalized manic patients on a double-blind basis. All three individuals showed clinical change both during and after the physostigmine period, which can be clearly delieated into three distinct phases. The behavioral modifications occurring during the physostigmine run did not qualitatively alter the underlying mania. The rebound phenomena, or postphysostigmine changes are discussed as a possiblce clinical index with which chemically to characterize the initial state of amine imbalance respondible for a given affective illness. The data are considered consistent with an adrenergic/dopaminergic/cholinergic balance hypothesis of affective disorders, and may provide a relevant link in understanding the interface or crossover between manic and schizoaffective illness. 28 references. (Author abstract)

230824 Fyro, Bengt; Petterson, Ulla; Sedvall, Goran. Department of Psychiatry, St. Goran's Hospital, S-112 81 Stockholm, Sweden **The effect of lithium treatment on manic symptoms and levels of monoamine metabolites in cerebrospinal fluid of manic depressive patients.** Psychopharmacologia (Berlin). 44(1):99-103, 1975.

Clinical effects, levels of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) in cerebrospinal fluid (CSF) and lithium levels in serum were examined in 13 manic-depressive patients acutely admitted because of a manic or hypomanic episode. Patients were examined before and 12 days after the beginning of lithium treatment. Manic scores were significantly reduced during treatment. The levels of 5-HIAA as well as HVA increased significantly during treatment. The HVA to 5-HIAA ratio was significantly reduced, indicating a more pronounced change in 5-HIAA than in HVA. The 5-HIAA and HVA levels before as well as after 12 days of treatment were significantly correlated. No significant correlation was found between manic scores and monoamine metabolites in CSF or between lithium level in serum and reduction of manic scores or elevation of monoamine metabolites in CSF in the relative small number of patients studied. 32 references. (Author abstract)

230827 Jori, A.; Dolfini, E.; Casati, C.; Argenta, G. Istituto di Richerche Farmacologiche "Mario Negri", Via Eritrea 62, I-20157 Milan, Italy **Effect of ECT and imipramine treatment on the concentration of 5-hydroxyindoleacetic acid (5HIAA) and homovanillic acid (HVA) in the cerebrospinal fluid of depressed patients.** Psychopharmacologia (Berlin). 44(1):87-90, 1975.

The influence of probenecid administration on 5-hydroxyindoleacetic acid and homovanillic acid concentrations in the cerebrospinal fluid (CSF) of depressed patients was studied before and after treatment with imipramine or electroconvulsive therapy (ECT). The average increase of the two metabolites in the CSF after probenecid was similar in the untreated depressed patients and in the same patients after both imipramine or ECT treatment. The treatment determined a significant increase in the CSF concentration of the acid metabolities also before the probenecid administration. 20 references. (Author abstract)

230990 Vanini, M.; Monteverdi, T.; Mase, G. B. Ospedale Psichiatrico Provinciale di Como, Como, Italy **/Treatment of depressive syndromes in involutional subjects./** Contributo alla terapia delle sindromi depressive nei soggetti in eta involutiva. Rassegna di Studi Psichiatrici (Siena). 64(3):435-445, 1975.

Trazodone was investigated for its resocializing effect in treating involutional depression syndromes with 18 patients over 50 years of age. Clinical evaluation of the effects was determined by Hamilton's scale at the beginning of treatment, and again after 7 and 15 days. The results showed that trazodone has both a short latency antidepressant effect and an almost immediate anxiolytic effect. Side-effects were much milder than those encountered with other tricyclic antidepressants. The fact that pyrosis occurred with i.v. administration of the drug indicates that more complex physiopathological mechanisms are brought into play than that of simple local "irritation.". 36 references.

230992 Monteverdi, T.; Vanini, M.; Mase, G. B. Ospedale Psichiatrico Provinciale di Como, Como, Italy **/A contribution to treatment of depressive syndromes: use of trazodone intravenously./** Contributo alla terapia delle sindromi depressive: uso del trazodone per via endovenosa. Rassegna di Studi Psichiatrici (Siena). 64(3):457-464, 1975.

Trazodone was investigated for its resocializing effect in treating depressive syndromes in a patient population from 22-50 years of age. The clinical evaluation of the results was done by means of the Hamilton Scale, administered at the beginning of treatment and after 7 and 15 days. The Ss were divided into groups of neurotic, endogenous and atypical depressives. With neurotic-reactive depression, there were four very good results, six good results, and four moderate results; with endogenous depression, there was one very good result and two unsatisfactory results; with atypical depressions, one result was very good, one was moderate, and two were unsatisfactory. The anxiolytic effect of trazodone was very good and very rapid. 15 references.

231035 Pecknold, J. C.; Ban, T. A.; Lehmann, H. E.; Klingner, A. Department of Psychiatry, McGill University, Montreal, Quebec **A clinical trial with nomifensin, a new antidepressant drug.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(4):304-308, 1975.

At the Tenth Annual Meeting of the Canadian Society of Clinical Pharmacology and Chemotherapy, held in Montreal in September 1974, an uncontrolled clinical trial with 10 depressed patients, which was conducted to identify the psychopathological symptoms which may be affected by nomifensin administration, and to reveal the possible adverse effects of the drug was discussed. Consistent statistically significant improvement was noted in the course of the clinical trial on all the assessment instruments used, and all patients improved while receiving nomifensin. Most of the therapeutic changes were seen within the first 3 weeks of treatment, and they included improvement of depression, as well as of hostility, a symptom which usually remains unaffected by tricyclic antidepressant drugs. To verify the favorable therapeutic effects of nomifensin in depressed psychiatric patients, a standard controlled clinical trial was begun; and to verify the action mechanism of nomifensin, a study employing the probenecid technique and the measurement of spinal homovanillic acid (HBA) and 5-hydroxyindoleacetic acid (5HIAA) concentration was planned. 3 references. (Author abstract)

231368 Arnone, A.; Del Priore, M.; Menduni, G.; Modonesi, C. Ospedale Psichiatrico Provinciale, Cogoleto, Italy **/The little known therapeutic properties of imipramine in manic states of cyclothymic psychoses./** Sulle poco note proprieta terapeutiche dell'imipramina negli stati maniacali della psicosi ciclotimica. Neuropsychiatria (Genova). 30(1-2):127-131, 1974.

The therapeutic properties of imipramine in treating manic states of cyclothymic psychoses are discussed. Doses of

imipramine varying between 150mg and 200mg/day caused a rapid reduction and subsequent disappearance of the manic state. The drug can also be used in preventive treatment for avoiding the appearance of pathological dysthymic episodes. One case is reported of lithium treatment associated with small doses of impiramine. It is concluded that imipramine is one of the most effective antidepressants, and is also capable of giving a true equilibrium to mood tone. 15 references.

231401 McCallum Peter; Meares, Russell. Dept. of Psychiatry, University of Melbourne, Austin Hospital, Heidelberg, Vic. 3084, Australia **A controlled trial of maprotiline (Ludiomil) in depressed outpatients.** Medical Journal of Australia (Sydney). 2(1):392-394, 1975.

Maprotiline, a new tetracyclic antidepressant, was compared with amitrptyline and placebo in a double-blind study of psychiatric outpatients. Amitriptyline was significantly more effective than placebo in its global effect on depression. Maprotiline emerged as neither inferior to amitriptyline nor superior to placebo. It is concluded that methodological difficulties prevented an adequate assessment of the anxiolytic activity of maprotiline. 9 references. (Author abstract modified)

231610 Lion, John R.; Penna, Manoel W. Dept. of Psychiatry, Institute of Psychiatry and Human Behavior, Univ. of Maryland School of Medicine, Baltimore, MD 21201 **Concepts of impulsivity: a clinical note.** Diseases of the Nervous System. 36(11):630-631, 1975.

Psychotropic agents which have been used to treat impulsivity are reviewed. It is noted that impulsivity is a behavioral trait which in large part relates to emotional and physiologic maturation, and to those ego functions which facilitate the individual's ability to delay action and promote the formation of inhibitory processes. Therapeutic intervention in these functions requires clinical awareness of both psychological and organic parameters. 15 references.

231611 Benson, Robert. no address **The forgotten treatment modality in bipolar illness: psychotherapy.** Diseases of the Nervous System. 36(11):634-638, 1975.

Data from a study of 31 bipolar patients treated with combined lithium prophylaxis and psychotherapy for up to 41 months are presented. The grave prognosis of untreated bipolar illness and the improved prognosis with lithium prophylaxis alone are reviewed. An even more improved prognosis when lithium prophylaxis is combined with psychotherapy is demonstrated, and reasons why lithium prophylaxis alone still predicts a grave outcome are discussed. Psychotherapy is important to: (1) keep the patient motivated to continue lithium treatment; (2) ease the fear and terror of the manic episode; (3) allow the patient to explore new avenues of creativity; and (4) allow the therapist to monitor the patient's mood as an early detection of falling serum lithium levels. 44 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

226187 Ghose, Karabi; Turner, Paul; Coppen, Alec. St. Bartholomew's Hospital, London EC1A 7 BE, England **Intravenous tyramine pressor response in depression.** Lancet (London). No. 7920:1317-1318, 1975.

Tyramine dose/pressor response curves were determined for 19 patients with primary depressive illness. In the depressive group, significantly lower doses of tyramine were required to elevate the systolic blood pressure by 30 mm. Hg. There was no correlation found between age, body weight, and tyramine dose/pressor response. Both male and female patients were found to differ significantly from their control groups; i.e.,the tyramine dose required to elevate systolic blood pressure in depressives was less than in the control groups. 15 references. (Author abstract modified)

226410 d'Elia, G.; von Knorring, L.; Marcusson, J.; Mattsson, B.; Perris, C.; Persson, G. Dept. of Psychiatry, University of Gothenburg, S-413 45 Gothenburg, Sweden **A double blind comparison between doxepin and diazepam in the treatment of states of anxiety.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:35-46, 1974.

An 8 week double-blind trial was carried out to compare doxepin and diazepam on randomly chosen outpatients with symptoms and signs of anxiety, tension and depression. It was found that both drugs reduced all symptoms and signs. Comparison of the total number of signs showed a significant difference in favor of doxepin. No significant differences between the drugs in the assessment of the total number of symptoms or social functioning were found. Among those who completed the investigation side-effect were found to be mild and equal in both groups. An increase in weight was noted in the doxepin group. It is concluded that doxepin and diazepam in small doses have comparable anxiolytic properties. 10 references. (Author abstract modified)

227141 Abe, Kazuhiko. Department of Psychiatry, Osaka City University Medical School, Abenoku, Osaka, Japan **Sulpiride in depressive school phobic children.** Psychopharmacologia (Berlin). 43(1):101, 1975.

The use of sulpiride in depressive school phobic children (9-17 years old) is discussed. Ten of the 16 children treated returned to school within a few days; their anxious, depressive and autonomic symptoms disappeared within a week. In three of the remaining children, school phobia persisted, although the accompanying depressive and paranoid symptoms ameliorated and according to the mother, behavior at home returned to nearly normal. The remaining children showed no significant change on sulpiride. Since early return to school is essential for the child's subsequent adjustment at school, it is preferable to use drugs which are rapid acting, like sulpiride. In view of the absence of serious side-effects like blood and liver toxicity reported occasionally with imipramine, sulpiride is to be used first, rather than imipramine, if pharmacotherapy is considered necessary. 6 references.

227825 Johnson, Walter C. 132 Pine Street, Hanover, MA 02339 **A neglected modality in psychiatric treatment -- the monoamine oxidase inhibitors.** Diseases of the Nervous System. 36(9):521-525, 1975.

The history, pharmacology, side-effects, and indications for use of the monoamine oxidase (MAO) inhibitors are reviewed. It is suggested that the MAO inhibitors are presently being used infrequently because of reports of severe and dangerous side-effects such as toxic hepatocellular damage and hypertensive crises, and also because of studies which have cast doubt upon the efficacy of these drugs. Clinical evidence is reviewed which demonstrates that the MAO inhibitors are very useful when the proper indications for their employment are observed and are relatively safe provided that appropriate precautions such as the avoidance of cheese and other foods high in tyramine content are taken by patients being treated with these compounds. It is argued that MAO inhibitors are the agents of choice in atypical depressions associated with anxiety, phobic and hysterical symptoms, and depressive ill-

nesses which have failed to respond to tricyclic antidepressants. 20 references.

227914 General Practitioner Research Group. Twickenham, England **A single-dose anti-anxiety drug: a report from the General Practitioner Research Group.** Practitioner (London). 215(1285):98-101, 1975.

A double-blind comparison trial between clorazepate (a new benzodiazepine drug) and diazepam for treatment of anxiety symptoms is reported. Patient response to clorazepate treatment was recorded on the severity of symptoms as measured by three means. Clorazepate in the single dose of 15mg at night had similar antianxiety effects to those of diazepam in a dose of 5mg three times daily. There were no differences between the two drugs with respect to rapidity of action, overall effectiveness, and incidence, nature and severity of side-effects. The single nightly dose of clorazepate, however, is particularly convenient for use in general practice. Specific side-effects and patient data are discussed.

228207 General Practitioner Research Group. no address **A combination of anti-anxiety drugs: report from the General Practitioner Research Group.** Practitioner (London). 215(1286):230-233, 1975.

The effect of combining two antianxiety drugs, chlordiazepoxide and pimozide was examined. Ss were 58 patients whose symptoms of anxiety had been present for at least one week. The addition of pimozide to chlordiazepoxide did not result in a more rapid antianxiety effect, an enhanced effect, a "sparing" of chlordiazepoxide dosage, or a reduced incidence of side-effects. It is concluded that the combination of pimozide with chlordiazepoxide has no advantage over chlordiazepoxide alone.

229025 Yamamura, Hitoshi. Department of Neuropsychiatry, Nagoya Municipal University School of Medicine, Japan **Clinical experience in using cloxazolam (Sepazon).** Medical Consultation & New Remedies (Tokyo). 12(1):165-176, 1975.

The effect of cloxazolam on 30 outpatients with various types of psychiatric troubles was studied. The patients were treated with cloxazolam for 7 weeks. The effectivity rate of the drug was 60%. It was found effective on melancholia and neurotic depression and less effective on circular depression and hypochondriasis. Side-effects, such as drowsiness, dizziness, weakness and dry mouth, were observed; most of these side-effects disappeared without termination of the drug. 9 references.

229451 Zitrin, Charlotte Marker; Klein, Donald F. Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Imipramine, behavior therapy, and phobia.** Psychopharmacology Bulletin. 11(4):41-42, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, a study of the effectiveness of combined imipramine and behavior therapy, combined placebo and behavior therapy, and supportive psychotherapy and imipramine in agoraphobic, phobic neurotic, and mixed phobic Ss was reported. Agoraphobic and mixed phobic Ss responded much more favorably to imipramine treatment regimens than placebo regimens, while with phobic neurotics, no differences occurred between regimens. Findings indicate that the therapeutic effect of imipramine relates to its elimination of the spontaneous panic attacks in agoraphobics. Agoraphobia, unlike neurotic phobia, is a core phasic disorder and as long as this remains uncontrolled, patients believe that psychotherapeutic intervention is of little or no value. Imipramine allows this control and leads to response to psychotherapy which reduces the anticipatory anxiety, so that the S can confront phobic situations. Over 70% of the patients maintained significant improvement during the first followup year. 1 reference. (Journal abstract modified)

229515 Lankosz, Jan; Weselucha, Piotr. Klinika Chorob Wewnetrznych Instytutu Medycyny Wewnetrznej AM, Krakow, Poland **/Doxepin, a new antidepressant drug for patients in the internal medicine clinic./** Doksepina -- nowy lek antydepresyjny w klinice chorob wewnetrznych. Przeglad Lekarski (Warszawa). 31(5):573-577, 1974.

A clinical evaluation of the new antidepressant drug doxepin was carried out in the internal medicine ward and in the internal and psychosomatic medicine outpatient department of a Krakow clinic. Thirty inpatients and 26 outpatients participated in the study. The use of the drug as a basic therapeutic agent and as an accessory agent is discussed. Its nontoxic effects and its side-effects are also summarized. It is concluded that the drug is an effective basic or supplementary agent for somatogenic, endogenous, and psychogenic depressions. 20 references. (Journal abstract modified)

229559 Pinto, Francesco; Ferro, Filippo Maria; Gambi, Domenico. Clinica delle Malattie Nervose e Mentali, Universita Cattolica del S. Cuore, Rome **/The treatment of psychotic anxiety./** Il trattamento dell'angoscia psicotica. Rivista di Psichiatria (Roma). 10(1):105-110, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, the treatment of psychotic anxiety with long-acting neuroleptic agents was discussed. Long-acting drugs may arrest the precipitation of psychotic attacks in patients with no previous psychiatric history, and thereby avoid the stigma of hospitalization. With patients whose disorders are more advanced, hospitalization in an open ward is possible. In addition, the use of these drugs prevents disturbances in the families of patients who are living at home. 10 references.

230015 Howlett, Lynda; Markoff, Richard A. University of Hawaii School of Medicine, Honolulu, HI **Clinical experiences with antidepressant drugs in the treatment of anxious-phobic patients.** Comprehensive Psychiatry. 16(5):461-465, 1975.

Four clinical cases are presented that appear to fit into the syndrome of panic anxiety with secondary anticipatory anxiety and phobic development that has been described by Klein and others, and treatment with tricyclic antidepressants is reported. Results suggest that antidepressant drugs are highly useful in the treatment of this syndrome. 13 references. (Author abstract modified)

230818 Holowiecki, Jerzy; Hese, Robert; Stella, Beata. ul. Dworska 2 40-584 Katowice-Brzynow, Poland **/Effectiveness of Sinequan (Doxepine) in the treatment of neurotic and pseudoneurotic syndromes./** Skutecznosc Sinequanu (Doxepiny) w leczeniu zespolow nerwicowch i pseudonerwicowych. Wiadomosci Lekarskie (Warszawa). 27(21):1861-1864, 1974.

The results of treatment of 26 patients with neurotic or pseudoneurotic syndromes during various somatic diseases with Sinequan (Doxepine) are described. The drug was administered during 2 weeks in daily doses of 30mg and during the subsequent 2 weeks in daily doses of 75mg. Significant improvement was observed in 14 cases, and improvement in 10 cases, following drug treatment. Statistical analysis of symp-

toms evaluated by the Hamilton scoring system indciated highly significant improvements. Significantly better results were obtained after higher doses. Slight side-effects disappeared after the first days of treatment and were not stronger following daily doses of 75mg. 10 references. (Journal abstract modified)

231036 Lapierre, Y. D. Pierre Janet Hospital, 20 Pharand St., Hull, Quebec, Canad **Clinical and physiological assessment of chlorazepate, diazepam and placebo in anxious neurotics.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(4):315-322, 1975.

At the Tenth Annual Meeting of the Canadian Society of Clinical Pharmacology and Chemotherapy, held in Montreal in September 1974, a 28 day double-blind assessment of chlorazepate dipotassium, diazepam and placebo, which was performed on 30 outpatient neurotics with the primary symptom of anxiety was discussed. Acute, subacute and more chronic effects of the drug were assessed after 3 hours, 14 days and 28 days of drug administration. A battery of psychiatric ratings as well as physiological and psychophysiological assessments were done at each period. The psychometric assessments showed a trend for diazepam to be the most anxiolytic of the three drugs, followed by chlorazepate and then placebo. These measurements did not reach uniform statistically significant differences. Psychological measurements demonstrated the same trends, but some of these reached statistically significant levels. These parameters also indicated a slightly different mode of action of the two drugs at equimolecular doses. Diazepam depressed baseline and stimulation arousal, whereas chlorazepate decreased baseline central nervous system (CNS) arousal, but facilitated central nervous system response upon stimulation. 16 references. (Author abstract)

231603 DeSousa, Alan; Choudhury, P. C. Grant Medical College, Bombay-8, India **Double blind trial of "Sintamil" in depression.** Indian Journal of Psychiatry (Madurai). 16(2):159-164, 1974.

A double-blind trial of Sintamil and imipramine in the treatment of depression is reported. Subjects were 56 adult depressives who were hospital outpatients in Bombay. They were treated for 4 weeks according to a predetermined random order. An improvement in the depressive state was observed in 69% of the patients treated with Sintamil compared with 41% of those treated with imipramine. In cases of severe depression 90% responded favorably to treatment with Sintamil, compared to 29% of those treated with imipramine. The incidence of side-effects with Sintamil was lower, and the side-effects were mild in comparison to imipramine, where the severity of side-effects required discontinuation of treatment in seven cases. It is concluded that, because of the higher percentage of favorable response and the lower incidence of side-effects, Sintamil is an effective agent in the treatment of depression. 5 references. (Author abstract modified)

231983 Welbel, Leszek. Instytut Psychoneurologiczny, Al. Sobieskiego 1/9, 02-957 Warsaw, Poland **/Treatment of neurotic syndromes with tranquilizers./** Leczenie zespolow nerwicowych srodkami trankwilizuj acymi. Psychiatria Polska (Warszawa). 8(4):415-420, 1974.

The results are presented of a controlled study comparing the effects of treating neurotic syndromes with benzoctamine, medazepam, and Tempidon in 127 patients and with oxazepam and a placebo in 61 patients. Treatment effectiveness was evaluated by means of a specially prepared symptom inventory. Medazepam was the most effective drug tested, followed closely by benzoctamine. Benzoctamine had the most universal mode of action, whereas medazepam had a tranquilizing effect. The incidence of side-effects was greatest with medazepam. 14 references. (Journal abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

225766 West, William L. Department of Pharmacology, College of Medicine, Howard University, Washington, DC **Drug action in management of hypertension.** Urban Health. 4(3):36-41, 1975.

The treatment of hypertension by drug action is discussed, and mechanisms of drug action are investigated as a means of investigating possible etiology of the syndrome. Types of hypertension considered by etiological grouping include primary/essential, secondary/renal, adrenal, neurogenic, coarctation of aorta, and toxemia of pregnancy. A summary of drug action in therapy for hypertension is given for chlorothiazide, diazoxide, hydralazine, alphamethyl dopa, reserpine, guanethidine, ganglion blockers, propranolol, and phentolamine; certain contraindicated drug combinations are mentioned. 15 references.

226413 Mattsson, B.; Mjorndal, T.; Oreland, L. Dept. of Psychiatry, University of Umea, S-901 85 Umea, Sweden **Plasma levels of chlorprothixene in alcoholics.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:71-74, 1974.

An investigation was made to study the metabolism of the thioxanthene preparation chlorprothixene in the presence of alcohol. Chlorprothixene is widely used in the treatment of alcoholics, and any possible changes in its metabolism are judged to be of clinical interest. Thirty mg. of chlorprothixene was given to three groups of patients: 1) patients in a state of acute alcoholic intoxication, 2) patients with a diagnosis of chronic alcoholism but in a sober phase, and 3) a control group. No differences in plasma concentrations or rates of elimination of the drug were observed. 5 references. (Author abstract modified)

226414 Mattsson, B.; von Schoultz, B. Dept. of Psychiatry, University of Umea, S-901 85 Umea, Sweden **A comparison between lithium, placebo and a diuretic in premenstrual tension.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplementum 255:75-84, 1974.

Because the premenstrual phase in most women is accompained by varying degrees of psychic and/or somatic distress and premenstrual tension is characterized by anxiety, depression, irritability, headache, or feeling of swelling, an investigation was undertaken of three treatment modalities. Eighteen women with mild and moderate premenstrual symptoms participated in a double-blind crossover trial involving placebo, a diuretic drug, and lithium. It is concluded that all drugs ameliorated the symptoms: placebo most, diuretic drug and lithium less, and a diuretic effect of lithium accompanied improvement in some cases. It is noted that these results are valid for women with mild and moderate premenstrual symptoms. 15 references. (Author abstract modified)

226478 Cole, Jonathan O.; Branconnier, Roland J.; Martin, Gary F. Institute of Research and Rehabilitation, Boston State Hospital, Boston, MA 02124 **Electroencephalographic and behavioral changes associated with papaverine administration in healthy geriatric subjects.** Journal of the American Geriatrics Society. 23(7):295-300, 1975.

A double-blind crossover procedure was used to evaluate the effects of papaverine hydrochloride on the EEG, cognition, mood and psychologic test performance of ten healthy geriatric volunteers. During the 2 week period, each subject was tested four times: before and after receiving papaverine and before and after receiving placebo. Period analysis revealed that a 300 mg. dose of papaverine increased EEG alpha activity and decreased the beta-2 range. Baseline values for six mood factors, short-term memory, complex problem solving, and attention were not altered significantly by either drug or placebo. Results of the Subject Paced Digit Symbol Substitution Test indicated that papaverine may produce some improvement in simple cognitive functioning. No adverse effects were associated with the use of papaverine. 19 references. (Author abstract modified)

226960 Burke, David; Hammond, Charles; Skuse, Nevell; Jones, Richard F. Division of Neurology, Prince Henry Hospital, Little Bay, N.S.W. 2036, Australia **A phenothiazine derivative in the treatment of spasticity.** Journal of Neurology, Neurosurgery, and Psychiatry (London0. 38(5):469-474, 1975.

The efficacy of a selective fusimotor suppressant, the phenothiazine (0)-10-(3-dimethylamino-2-methylpropyl)2-valeroylphenothizine, has been assessed in a double-blind crossover trial in eight patients suffering from cerebral spasticity and one patient suffering from spinal spasticity. Dosage was 40mg daily. Independent clinical and electromyographic methods of assessment were used. The active agent produced a small but significant reduction in spasticity, although this was of clinical value in only a few patients. There were few side effects. It is recommended that further studies using higher dosages be undertaken. 15 references. (Author abstract)

227330 Zwerling, Israel; Plutchik, Robert; Hotz, Margaret; Kling, Ruth; Rubin, Leo; Grossman, Joel; Siegel, Barbara. Department of Psychiatry, Hahnemann Medical College, Philadelphia, PA **Effects of a procaine preparation (Gerovital H3) in hospitalized geriatric patients: a double-blind study.** Journal of the American Geriatrics Society. 23(8):355-359, 1975.

The effects of Gerovital H3 (procaine hydrochloride) on geriatric patients were assessed in a double-blind study. Moderately severe organic symptoms were rated in subjects with a mean age of 73 years. Five ml injections were given intramuscularly three times a week for 6 weeks; dosages were doubled for the second 6 weeks. Nine Gerovital and 10 control subjects finished the first 6 weeks, and 6 Gerovital and 7 control subjects completed the entire 12 week study. Patients were evaluated on measures of interpersonal functioning, cognitive ability, psychiatric symptoms and urine and blood chemical findings. Results show that differences between the two groups were small, insignificant, and followed no consistent pattern. It is concluded that Gerovital H3 had no ameliorative effect on either psychological or physiological functioning. 14 references. (Author abstract modified)

227550 Leonard, D. P.; Kidson, M. A.; Brown, J. G. E.; Shannon, P. J.; Taryan, S. Monash University Clinical Unit, Larundel Hospital, Plenty Rd., Bundoora, Victoria 3083 **A double blind trial of lithium carbonate and haloperidol in Huntington's chorea.** Australian and New Zelaand Journal of Psychiatry (Carlton). 9(2):115-118, 1975.

Six patients with a family history of Huntington's chorea (HC) participated in a double-blind crossover trial involving four treatments: lithium carbonate, haloperidol, lithium carbonate and haloperidol, and placebo. Each treatment was administered for 3 weeks, and assessments were made at the end of each for chorea and a number of psychological variables. None of the treatments significantly affected chorea measurements, but levels of irritability, frequency of angry outbursts and depression were influenced in some patients. Results indicate that three Ss improved on a combination of lithium cabonate and haloperidol, while the remaining three did not. Haloperidol alone significantly raised depression ratings above levels for other treatments, including placebo. It is suggested that lithium carbonate and haloperidol together should be seriously considered in the treatment of HC when patients are excessively irritable and impulsive. 9 references. (Author abstract)

227570 Casey, Daniel E.; Denney, Duane. Butler Hospital, 333 Grotto Avenue, Providence, RI 02906 **Deanol in the treatment of tardive dyskinesia.** American Journal of Psychiatry. 132(8):864-867, 1975.

A case history is given of a patient who developed severe tardive dyskinesia after the termination of long-term phenothiazine therapy and who was successfully treated with deanol, a possible precursor of acetylcholine. Physiological measurements were obtained to quantify the clinical course. The practical and heuristic implications of these observations are discussed, and further considerations of therapy directed toward enhancement of cholinergic activity in the central nervous system are suggested. 9 references. (Journal abstract modified)

227571 Huestis, Robert D.; Arnold, L. Eugene; Smeltzer, Donald J. Dept. of Psychiatry, Naval Regional Medical Center, Norfolk, VA **Caffeine versus methylphenidate and d-amphetamine in minimal brain dysfunction: a double-blind comparison.** American Journal of Psychiatry. 132(8):868-870, 1975.

The efficacy of pure caffeine, methylphenidate, and d-amphetamine in children with minimal brain dysfunction were compared in a double-blind study in the hopes of finding a safer medication for hyperkinetic children than the Schedule II stimulants. The slight improvement with caffeine was not significantly better than placebo. Both prescription drugs resulted in significant improvement and were significantly superior to caffeine. It is suggested that the discrepancy between these results and an earlier, more optimistic report may stem from the use in this study of pure caffeine rather than whole coffee. 5 references. (Journal abstract modified)

227711 Carney, M. W. P. Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England **Folate-responsive schizophrenia.** Lancet (London). 2(7928):276, 1975.

In a restrospective survey of psychiatric inpatients with a low serum folate at admission, a group given folate supplements randomly was compared with a comparable group of patients who were not given folate. The treatment group included 3 patients with schizophrenia, 10 with endogenous depression, and 7 with organic psychoses; the nontreatment group consisted of 10 patients with schizophrenia, 8 with endogenous depression, and 12 with organic psychoses. Ss were observed for time periods ranging from 23-100 days. Folate treated patients spent significantly less time in hospital than those not given folate, a difference not seen in low folate patients with other psychiatric diagnoses. 3 references.

227750 Morrant, J. C. A. Mt. Pleasant/Fairview Community Care Team, Vancouver, British Columbia **Medicines and mental illness in old age.** Canadian Psychiatric Association Journal (Ottawa). 20(4):309-312, 1975.

The use of drugs in treating mental illness in the elderly is discussed, and psychiatric side-effects of drugs commonly used with elderly patients are reviewed. The psychosocial syndrome of analgesic abuse can be found singly or combined with alcohol dependence, abuse of purgatives, and bromism. Cough mixtures which contain phenylpropanolamine could precipitate a psychiatric illness. Overprescribing of the following drugs is widespread in hospitals and nursing homes: diuretics, digitalis, hypotensives, oral hypoglycemics, cerebral vasodilators, and antibiotics. The following psychotropic drugs can cause or aggravate a psychiatric disturbance: barbiturates, methylphenidate, the monoamine oxidase inhibitor group of antidepressants; the tricyclic antidepressants, amitriptyline and trimipramine, antipsychotics and antiparkinsonians. 8 references.

227766 Rimestad, Soren. Dikemark Hospital, N-1385, Solberg, Norway **Clinical physiognomy of chlorprothixene and clopentixol.** Acta Psychiatrica Belgica (Bruxelles). 74(5):491-499, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, studies of the use of chlorprothixene and clopentixol were reviewed. Chlorprothixene is being used successfully in a variety of psychiatric conditions including schizophrenia, mania, depression, psychopathy and alcoholic psychoses. Side-effects are usually dose related and limited to the beginning of the treatment. Clopentixol, despite its greater sedative efficacy than chlorprothixene, is not considered a broad spectrum neuroleptic because of its stronger antipsychotic and extrapyramidal effects. It is mainly used in schizophrenia but has also been successful in treating other psychoses.

227806 Abe, Takejiro. Department of Internal Medicine, Tokyo Police Hospital, Japan **Clinical experience in using sulpiride for internal psychosomatic illness.** Medical Consultation & New Remedies (Tokyo). 12(2):311-319, 1975.

The effect of sulpiride on internal psychosomatic disorders was studied, based on an experiment in which 30 outpatients (10 with hypertension, 2 with hypotension, 1 each with cardiac neurosis, autovegetative Stigmata, dysthyroidism, cervical arm syndrome, presenile depression, sequelae of brain injury, diabetes insipidus and chronic bronchitis, 5 with chronic gastritis and gastroenteritis, 4 with gastric ulcer and 1 with esophageal cancer) were treated with the drug (150 mg/day) for 4 to 10 weeks. Sulpiride was extremely effective in 37.9% of the patients, and was at least somewhat effective rate was 44.8%. The drug seemed to be more effective in patients with digestive organ disturbances. Although specific symptoms ameliorated by sulpiride and speed of appearance of effects could not be determined, the drug was often effective in patients who failed to show improvement with other antidepressants. 6 references.

227818 Ogawa, Nobuya. Department of Pharmacology, Kyushu University, Japan **Pharmacotherapy of psychosomatic cases.** Popular Medicine (Tokyo). No. 62:87-90, 1975.

The methodology of psychopharmacotherapy for psychosomatic diseases is discussed. Psychopharmacotherapy for gastric ulcer and essential hypertension is considered.

227923 West, Shelia K. Health Svcs. Research and Development Ctr., Johns Hopkins Medical Institutions, Baltimore, MD 21205 **Providers as prescribers: attitudes toward aspects of prescribing and their relationship to management of hypertension in the elderly.** Gerontologist. 15(4):317-319, 1975.

At Symposium: Health Care of the Aged, a part of the annual meeting of the Gerontological Society held in Portland in October 1974, a paper was presented in which three variables measuring attitudes toward prescribing drugs for hypertensive elderly patients were examined in terms of differences in provider type and setting. It was hypothesized that the provider's decisions regarding drug therapy would be influenced by numerous factors, including sources of information on drugs, dimensions of quality and frequency of provision, and patient drug education. Results indicate that major differences were noted in use of literature and industry sources of drug information between physicians and nonphysician providers. A general overall concern for lack of care in prescribing was not shown to be related to the more specific concerns of adverse drug reaction and excessive prescribing for the elderly. Suggestions were also made for further research into differences in types of setting and practice. 7 references. (Author abstract modified)

227924 Hoey, John R. Health Services Research and Development Center, Johns Hopkins Medical Institutions, Baltimore, MD 21205 **Management of the elderly hypertensive in four practice settings.** Gerontologist. 15(4):320-325, 1975.

At Symposium: Health Care of the Aged, a part of the annual meeting of the Gerontological Society held in Portland in October 1974, a paper was presented in which patient and provider characteristics were analyzed in four settings described in the literature as illustrating patterns of care for the aged. A special study was made among the elderly hypertensive population using chart reviews and resident questionnaires. Approximately 75% of the hypertensives were shown to have controlled blood pressure after a minimum of 6 months of care, with the tendency being toward control from noncontrol, and with the Black inner-city group practice having the greater degree of change from noncontrol to control. Patients least educated and least satisfied with care tended to experience less favorable changes in diastolic pressures and specific setting appeared to make a difference in control. A major single provider as opposed to several providers did not affect control, and there appeared to be limited use of the newer types of drugs. Suggestions are also made for a larger study. 8 references. (Author abstract modified)

228074 Nishida, Hirofumi; Kuramitsu, Masayuki. Kuramitsu Hospital, Japan **A case of Gilles de la Tourette's syndrome.** Clinical Psychiatry (Tokyo). 17(7):727-736, 1975.

A typical case of Gilles de la Tourette's syndrome is reported, noteworthy due to the severity of aggressiveness with tics and coprolalia. The aggressivness was evaluated from a psychopathological viewpoint. The tic was found to be related to obsessive phenomena and impulsive behavior. Nighttime sleep electroencephalograms showed the tic to be present during a sleeping period, occurring frequently during rapid eye movement sleep. Haloperidol was an effective drug for this case. 44 references. (Journal abstract)

228091 Benoit, O. Laboratoire de'Etude du Sommeil, Centre de Recherches Neurophysiologiques, Unite 3 de l'INSERM, 47, bd de l'Hopital, 75634 Paris Cedex 13 **/Sleep and its disturbances in the child: contributions of electrophysiology./** Le sommeil de l'enfant et ses troubles: apports de l'electrophysiologie. Perspectives Psychiatriques (Paris). 2(51):133-138, 141-145, 1975.

The contributions of electrophysiology to knowledge about sleep and its disturbances in children are discussed. Sleep in the normal child is characterized by a predominance of deep

slow wave sleep at the beginning of the night, an increase in paradoxical sleep in the last third of the night, and the cyclic structure of sleep. The composition of sleep varies with age. The first cycle of the child's sleep is immature. Enuresis, somnambulism, nocturnal fright, and somniloquy are the major symptoms of sleep disturbances in the child over three years of age. Paroxysmal disturbances occur in a particular physiological state by interrupting or following slow wave deep sleep. The medication used in treating sleep disturbances is varied. In severe disturbances, diazepam is often employed. It is felt that hypnotics should be avoided. Modification of the anxiety causing the disturbance is viewed as being more important than obliteration of the symptom. Anxiolytic treatment improves sleep. 17 references.

228241 Titton, Joao Alceu; Boaretti, Antonio Carlos; De Almeida Luiz, Albano M. C.; Rachid, Acir. Rheumatology Service, Clinical Dept., Federal University of Parana, Brazil **Therapy of anxiety in patients with rheumatic disease: crossover double-blind study comparing lorazepam with placebo.** Psychosomatics. 16(3):120-123, 1975.

A controlled double-blind crossover study was designed to compare lorazepam (L) with placebo in the therapy of anxiety in patients with rheumatic/arthritic disorders and other chronic medical conditions, in such a way that all patients would receive both treatments sequentially. Lorazepam at a dose of 2mg/day in divided doses, adequately controlled anxiety and was well tolerated. Placebo had much less effect, and the patients' status deteriorated when placebo was substituted for L in the second 2 week phase (the crossover period). Somnolence occurred in eight patients, including six in the L and two in the placebo phase of treatment. One patient complained of dizziness on L; one patient experienced nausea, and one experienced diarrhea on placebo. 7 references. (Author abstract modified)

228242 Ananth, J. St. Mary's Hospital, 3830 Lacombe Ave., Montreal, P.Q. H3T 1M5 **Psychopharmacology and psychosomatic illness.** Psychosomatics. 16(3):124-128, 1975.

The place of pharmacotherapeutics in the treatment of psychosomatic illnesses was discussed in terms of the principles of psychosomatics and psychiatry. Endogenous anxiety, a clear indication for pharmacotherapy, was viewed as a causal component of every illness. A neurophysiological model of psychopathology and psychophysiological disorders was described. In the pharmacotherapy of psychosomatic conditions, the choice between drugs with the same psychotropic activity depends on their somatic effects. Research on psychopharmacological remedies for asthma, gastrointestinal disorders, ulcerative colitis, and allergic disorders was reviewed. 59 references.

228243 Doyle, Larry N. South Dakota Human Services Center, Yankton State Hospital, Yankton, SD 57078 **Imipramine pamoate in depression.** Psychosomatics. 16(3):129-131, 1975.

The efficacy and safety of imipramine pamoate (IP) and imipramine hydrochloride (IH) were compared in a double-blind study of 26 patients with a diagnosis of moderate to severe psychotic or neurotic depression. Thirteen patients received single daily doses of IP (150mg capsules) and the other 13 patients received 50mg of IH three times per day. Both drugs were highly effective in reducing the severity of depressive symptoms. Global depression and Lehmann-Rockliff symptom severity ratings were reduced significantly from baseline values in each treatment group. Differences between results in the IH and IP groups were not statistically significant. Two patients treated with IH complained of dry mouth; adverse effects were not observed in any patient on IP. 6 references.

228311 Murata, Tadayoshi. Department of Neurology, Tenshi Hospital, Sapporo, Hokkaido, Japan **Tranquilization effect of beta-blockade Alprenolol: a clinical study.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(3):334-339, 1975.

The tranquilization effect of beta blockade Alprenolol on anxiety was studied, based on a clinical administration of this drug (75 mg/a day) for 1 week to 6 months to eight patients with anxiety neurosis, two with arteriosclerosis, one with schizophrenia, and three with chronic alcoholism who had anxiety complaints. The drug was found effective in the majority of patients and showed good effects on complaints related to heart, anxiety, tremor and abstinence symptoms of alcoholism. No side-effects were observed. 11 references.

228315 Hara, Toshio. Department of Psychiatry and Neurology, Kitazato University School of Medicine, Sagamihara, Japan **Comparative evaluation of flurazepam and nitrazepam for occasional insomniacs.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(1):97-103, 1975.

The effect of flurazepam and nitrazepam on insomnia was studied in 30 male patients with occasional insomnia. The opinions of the patients after were as follows: 1) nitrazepam induced drowsiness, but flurazepam did not; 2) both drugs caused sleep within the same time interval; 3) both drugs induced the feeling of having had a good sleep; 4) flurazepam had fewer negative side-effects. 18 references.

228431 Merrill, Diedre M. Rouse. United States International University **Cognitive effects of methylphenidate on hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-19134 HC$13.50 MF$5.00 129 p.

The effects of hyperkinesis in children and methods of coping with this disability were examined to determine if changes in performance on achievement, intelligence, and visuomotor perception tests could be attributed to methylphenidate therapy. Instruments included the Wechsler Intelligence Scale for Children, the Draw-a-Person test, the Wide Range Achievement Test, and the Bender-Gestalt Test. Other hyperkinetic Ss took placebos, thus giving a measure of the halo effect, while a control group of hyperkinetics received no medication. Results show that teachers reported significant improvement in behavior in drug treated Ss, and that the methylphenidate also produced improvement in their behavior according to parents. Over a 3 month period, methylphenidate did not improve Ss' level of cognitive functioning, academic achievement, or visuomotor perception. It is concluded that methylphenidate does not improve the child's cognitive functioning, academic skills or visuomotor perception, but that it does improve classroom and home behavior. (Journal abstract modified)

228686 Richards, William Alan. Catholic University of America **Counseling, peak experiences and the human encounter with death: an empirical study of the efficacy of DPT-assisted counseling in enhancing the quality of life of persons with terminal cancer and their closest family members. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-18531 HC$13.50 MF$5.00 305 p.

The value of dipropyltryptamine (DPT) assisted counseling in enhancing the quality of life of persons with terminal cancer and their closest family member was assessed. Ss receiving DPT and counseling experienced decreased feelings of guilt and a less significant decrease in the fear of death. Further, the families of Ss receiving DPT and counseling experienced greater decrease in emotional distress than families of control Ss. Peak experiences under DPT assisted counseling were defined and it was determined that peakers manifest more improvement than nonpeakers. However, the relatives of peakers did not evidence a strong trend for greater decrease in emotional distress. Implications of these findings for education are explored, especially in terms of alleviating the pathogenic effects of the "death taboo" in contemporary American society, and in promoting the process of self-actualization. (Journal abstract modified)

228726 Ford, Virginia Burke. University of Maryland **An investigation of the selection process and drug treatment of explosively aggressive adolescent females. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-18096 HC$13.50 MF$5.00 77 p.

The effectiveness of Dilantin as a treatment modality for delinquent adolescent females was evaluated, and the appropriateness of tests used to screen for episodic dyscontrol Ss was determined. Explosively aggressive females were divided into drug and nondrug groups, and each S completed a battery of tests including the Monroe Scale, the Lorr Outpatient Mood Scale and four subtests of the Wechsler Intelligence Scale on a pretreatment/posttreatment basis. A third group of matched females was selected for their nonaggressive behavior, and each S completed the same battery of tests as the aggressive Ss. It is concluded that explosively aggressive female adolescents show a significant improvement in behavior as a result of Dilantin treatment. The scale effective as a screening device in the selection of explosively aggressive Ss is the Teacher's Rating Scale for use in drug studies with children. The Monroe Scale and the Lorr Outpatient Mood Scale did not discriminate between aggressive and nonaggressive groups. (Journal abstract modified)

228750 Davis, John Everett. Boston University Graduate School **An experimental therapy and re-education program for alcoholics including chemotherapy with propranolol hydrochloride. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-20985 HC$13.50 MF$5.00 225 p.

The ability of combined group therapy and administration of propranolol hydrochloride to keep anxiety sufficiently low to enable alcoholics to remain sober and in treatment was evaluated. In a double-blind design, Ss received either propranolol or placebo. Ss were also assigned to a treatment group, and Ss who remained in treatment for 4 weeks or longer answered anxiety questionnaires developed by the Institute for Personality and Ability Testing, and gave subjective evaluations of performance. It is concluded that Inderal does help Ss remain in treatment for the first 4 weeks after detox, but not thereafter. Further, anxiety scores do not correlate with any behavior measured except time away from heavy drinking. Also, group leadership is significant for keeping alcoholics in treatment, but group leader's lower evaluations of improvement for Ss who drank is not significant. It is proposed that intervention is necessary to help Ss remain in treatment, particularly for the 4 weeks after detox. (Journal abstract modified)

228908 Lowenstam, Ilse. Alcoholism Treatment Program, Veterans Administration, Los Angeles, CA **Drug treatment in a rehabilitation center for chronic alcoholics.** Journal of Chronic Diseases. 28(7/8):431-434, 1975.

The efficacy of psychoactive drug therapy with chronic alcoholics was assessed, in particular, the efficacy and safety of mesoridazine in comparison with chlordiazepoxide. It is concluded that both mesoridazine and chlordiazepoxide provide effective relief from symptoms seen in chronic alcoholic patients during the withdrawal phase. No adverse effects were observed in patients treated with either drug. However, all parameters of drug efficacy employed demonstrate consistently that mesoridazine is the more effective agent. The most impressive improvements obtained with mesoridazine occurred in anxiety, depression, tension, general appearance, and feelings of guilt, worthlessness, and hopelessness. 1 reference. (Author abstract modified)

229037 Chapel, J. L.; Fahim, M. Room N118, University of Missouri Medical Center, Columbia, MO 65201 **The clinical application of laboratory animal experimental findings: treatment of hypersexualized behavior in a male.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):234-238, 1975.

A drug/steroid interaction demonstrated in animals was used as a therapeutic modality for a human reproductive syndrome as sociated with overproduction of sex hormones. A combination of vitamin B12 and phenobarbital was administered daily to a 16-year-old mildly retarded male with an abnormally high serum testosterone level who was having difficulty coping with his sexual urges. After 3 months of treatment, his testosterone level decreased significantly and his hypersexualized behavior with girls had been eradicated. There were no side-effects in physical appearance or general health. However, followup reports suggest that the reduction of serum testosterone levels in man by the administration of phenobarbital and B12 is a temporary phenomenon and is reversible. 6 references. (Author abstract modified)

229044 Kryspin-Exner, K.; Demel, I. Ludwig Boltzmann Institute for Addiction Research, Mackgasse 7-9, 1237 Vienna, Austria **The use of tranquilizers in the treatment of mixed drug abuse.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):13-18, 1975.

A series of studies is reported which was designed to determine the addictive potential of tranquilizers in the long-term therapy of alcohol and barbiturate abuse. With constant medical supervision, patients who were previously dependent on barbiturate type drugs did not independently increase their intake so as to become dependent on the tranquilizers. Findings suggest that tranquilizers can be safely given when there is constant medical supervision combined with psychotherapy in drug dependent persons. Uncontrolled long-term administration is to be rejected in all circumstances. Data are discussed in terms of principles of tranquilizer administration in the treatment of drug abuse and in the general population. 16 references. (Author abstract modified)

229053 Gittelman-Klein, Rachel. Child Development Clinic, Long Island Jewish-Hillside Medical Center, Long Island, NY **Recent advances in child psychopharmacology.** New York, Human Sciences Press, 1976. $12.95.

Diagnoses, psychopharmacological management, clinical management, and theoretical etiological considerations among children with minimal brain dysfunction (MBD), psychosis and

neurosis are reported. Stimulant treatment of children with MBD is stressed. Contents include reports of empirical investigations on long-term side-effects, dosage levels, the use of new drugs such as caffeine and imipramine, drug effectiveness in young preschoolers, and the nature of cognitive changes which occur in children clinically improved with stimulant treatment. The latest prospective study of hyperkinetic children into adulthood is summarized, and heuristic biological theories of MBD are included. Discussions on clinical pharmacological management of hyperkinetic children, psychotic children, and phobic children are presented with specific recommendations regarding optimal medication regimes, dosages, side-effects, and ancillary nonpharmacological treatment.

229083 Kohler, C.; Clere, J.; Girtanner, B. Pavillon Jean Dechaume, Hopital Sainte-Eugenie, F 69230 St Genis Laval, France **/The use of clonazepam in treating convulsive manifestations with encephalopathy in children: study of 28 cases./** Interet du clonazepam dans le traitement des manifestations convulsives avec encephalopathie chez l'enfant: a propos de 28 cas. Revue de Neuropsychiatrie Infantile etc. (Paris). 23(5-6):381-387, 1975.

The effect of clonazepam (RO-054023) on convulsive manifestations in 28 cases of profound encephalopathy in children was investigated. The initial dosage must be low, on the order of one drop per kilogram of bodyweight. The clinical effectiveness is very rapid, but is sometimes associated with annoying side-effects. Nausea occured in young children suffering from West's syndrome. Results were good in 8 cases, partial in 10, and null in 10. Clonazepam was relatively effective in treating Lennox syndromes. 15 references.

229091 Baekeland, Frederick; Lundwall, Lawrence K. Dept. of Psychiatry, SUNY, Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY 11203 **Effects of discontinuity of medication on the results of a double-blind drug study in outpatient alcoholics.** Journal of Studies on Alcohol. 36(9):1268-1272, 1975.

The effects of discontinuity of medication were examined in a double-blind study of outpatient alcoholics randomly assigned to groups receiving either an oxazepam protriptyline combination or a placebo. When analysis of data included patients who missed clinic visits, findings indicate no differences between drug and placebo groups. When only patients who took adequate levels of medication were considered, the drug group fared significantly better than placebo group. 29 references. (Author abstract modified)

229165 Hamel, Albert R.; Riklan, Manuel. Fordham University, New York, NY 10458 **Cognitive and perceptual effects of long-range L-Dopa therapy in Parkinsonism.** Journal of Clinical Psychology. 31(2):321-323, 1975.

The psychological effects of long-range L-Dopa therapy in Parkinsonism were investigated. A group of Parkinsonian patients was tested before L-Dopa therapy began, and again after approximately 42 months of treatment. Their scores before administration of L-Dopa were compared to those of a sample of age and sex equated normals, while long-range treatment scores were compared with those of another normal sample, again age and sex equated. Findings indicate significant differences between the pre-L-Dopa patients and their comparison group on the Critical Flicker Fusion (CFF) test, Digit Span, Rate of Manipulation, and Block Design tests, but only the latter two tests showed significant differences between long-range L-Dopa treated patients and their comparison group. The evidence suggested that L-Dopa helped the Parkinsonian in his performance on CFF, Digit Span, and Rate of Manipulation tests, by retarding anticipated age declines associated with such performance and observed in the test results of normals. 10 references. (Author abstract modified)

229295 Olds, Sally Wendkos. no address **/The problems and treatment of patients with Gilles de la Tourette's syndrome./** A nightmarish disease. "Terrible to have: terrible to live with". Today's Health. 53(9):40-43, 45, 1975.

The symptoms and treatment of Gilles de la Tourette's syndrome, an affliction characterized by coprolalia, echolalia, and a variety of bizarre muscular and vocal tics, are described. The work of Arthur K. and Elaine Shapiro in treating patients with this disease is described. Haloperidol has been effective in eliminating symptoms in about 25% of these patients. The dramatic effect of haloperidol is one basis for the current belief that Tourette's syndrome is physiological rather than psychological in origin. Many researchers feel that a chemical imbalance in the brain, probably an excess of dopamine, may be at the root of the disease. There are some indications that Gilles de la Tourette's syndrome is a neurological, hereditary disorder. Continuing research into etiology and treatment is described.

229315 Hollister, Leo E. Veterans Administration Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Drugs for mental disorders of old age.** Journal of the American Medical Association. 234(2):195-198, 1975.

Pathogenesis and diagnosis of mental disorders of old age are reviewed, and drug treatments for psychoses associated with aging are discussed. Major categories of drugs that have been used are outlined and their general purposes are indicated. Consideration is given to: 1) stimulants and analeptics; 2) drugs to increase cerebral blood flow; 3) drugs to treat associated functional disorders; and 4) drugs based on some specific hypothesized causes such as hormone imbalance or nutritional deficiency. Best results for treating symptoms of senile brain disease have been obtained with antipsychotic drugs, even though the treatment is symptomatic and the degree of benefit sometimes small. Drugs that alter disturbed brain metabolism may afford a new treatment approach. 11 references.

229368 Cox, J. R. Nether Edge Hospital, Sheffield, England **Double-blind evaluation of naftidrofuryl in treating elderly confused hospitalised patients.** Gerontologia Clinica (Basel). 17(3):160-167, 1975.

In a double-blind comparison between naftidrofuryl and placebo, progress of elderly confused patients was assessed on scales completed by the nurse, occupational therapist and physician. Naftidrofuryl treated patients improved significantly according to the scales, and no improvement was found for placebo treated patients. When the response to each treatment was compared, naftidrofuryl was found to be significantly better than placebo on both nurse and physician assessment. There was considerable variation among assessors, suggesting that different aspects of the patients' condition were measured. There was also considerable variation in patient response. Some improved on naftidrofuryl and some deteriorated; some improved on placebo and some deteriorated. Overall findings indicate that patients admitted to the hospital with confusional states benefit from treatment with naftidrofuryl. 6 references. (Author abstract modified)

229370 Botter, P. A.; Sunier, A. Sinai Centre, Psychiatric Hospital of the Central Society of Jewish Mental Health Care, Amersfoort, The Netherlands **Treatment of depression in geriatrics with Anafranil.** Journal of International Medical Research (Northampton). 3(5):345-351, 1975.

The influence of Anafranil on the symptomatology of depression was evaluated in an open trial in 39 hospitalized geriatric patients suffering from various types of depression. Within one week a marked decrease in the depressive symptoms was observed. This improvement reached its maximum after 3 weeks and remained at this level during the fourth week of treatment. At a daily dose of 30 to 50mg of Anafranil (mean: 40mg) the results were good in 19 and moderate in 8 patients In three patients there was no change in their depressive state. The drug was well tolerated, and no abnormalities were observed in the laboratory investigations. 9 references. (Author abstract modified)

229457 Salzman, Carl; Shader, Richard I.; Harmatz, Jerold S. Psychopharmacology Laboratory, Massachusetts Mental Health Center, Boston, MA **Response of the elderly to psychotrophic drugs: predictable or idiosyncratic?** Psychopharmacology Bulletin. 11(4):48-50, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, a study of factors that influence drug response in the elderly was reported, including altered drug sensitivity, heterogeneity of the geriatric population, and differences between the elderly and the young adult in the perception or reporting of internal mood states. Changes in the aging human body may alter its sensitivity to the clinical and toxic effects of a drug, and the elderly are particularly susceptible to the sedative effect of psychotropic drugs. Phenothiazines mixed with tricyclic antidepressants and alpha-adrenergic blocking agents combined with antipsychotic drugs may also cause untoward effects. Lithium carbonate, although an effective treatment, may also cause undesirable reactions. Gender and age may influence response to psychotropic drugs, and there are unique problems associated with evaluating drug efficacy with the elderly. Evaluation of idiosyncratic or regular drug effects and side-effects must be undertaken in the context of alterations in the manner of reporting internal mood by the elderly. 9 references. (Journal abstract modified)

229458 Prien, Robert F. Central NP Research Laboratory, VA Hospital, Perry Point, MD **A survey of psychoactive drug use in the aged in Veterans Administration Hospitals.** Psychopharmacology Bulletin. 11(4):50-51, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, a study of the use of psychoactive drugs by aged persons in Veterans Administration Hospitals, surveyed in 1276 patients with a primary diagnosis of mental illness and 1209 Ss not diagnosed as mentally ill, was reported. A total of 37% of the patients received either antipsychotic, antidepressant, or antianxiety drugs, including 56% of the Ss with psychiatric disorders and 16% of those with other disorders. Five drugs (thioridazine, chlorpromazine, diazepam, chlordiazepoxide and amitriptyline) accounted for 63% of the those used. A total of 16% of psychiatric patients and 2% of nonpsychiatric patients received combinations of two more psychoactive drugs. Age was a significant variable in drug prescription practices, particularly with antipsychotic compounds, with patients between 60 and 65 years receiving more than twice the dosage given to patients over 75 years. The need for further research on psychoactive drug therapy in the elderly is emphasized, particularly as it relates to organic brain syndrome and use of polypharmacy. (Journal abstract modified)

229459 Lehmann, Heinz E.; Ban, Thomas A. Division of Psychopharmacology, Department of Psychiatry, McGill University, Montreal, Quebec, Canada **CNS stimulants and anabolic substances in geropsychiatric therapy.** Psychopharmacology Bulletin. 11(4):51, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, the effects of CNS stimulants and anabolic substances on psychogeriatric patients were discussed, suggesting that there are two approaches for systematic attacks on the problem of pharmacotherapy in such persons. The clinical investigator may study empirically in geriatric patients the effect of psychotropic drugs whose pharmacotherapeutic profiles have already been established in other patient groups. He also may take his clues from results of pharmacological studies in animals and study drugs that have produced interesting effects on the CNS metabolism, for example, by dissolving lipofuscin or amyloid or by increasing glucose utilization, tissue respiration, or protein synthesis in animal brains. Both approaches should supplement each other. Ribonucleic acid (RNA) is probably ineffective in geriatric disorders, but anabolic substances involving steroid hormones and other recently developed compounds seem to offer promise in the field of secondary and even primary prevention. (Journal abstract modified)

229460 Jarvik, Lissy, F.; Milne, Judith F. University of California, Los Angeles, CA 90024 **Gerovital-H3 -- a review of the literature.** Psychopharmacology Bulletin. 11(4):51-53, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico, in December, 1974, the use of procaine, a common local anesthetic, in elderly patients was analyzed, focusing on the antiaging effects of Gerovital-H3 (GH3), the most recently developed of such compounds. Tests with animal and human clinical studies do not indicate that procaine or GH3 can reverse aging changes or prolong life, nor that they are of benefit in specific senile or arteriosclerotic degeneration disorders, either physical or mental. The most promising indication of benefit from such treatment is in elderly patients with mild to moderate depression. If procaine is shown to inhibit monoamine oxidase in vivo, there will be a rationale for its antidepressant activity. As a weak, reversible inhibitor, procaine would be safer than the strong, irreversible monoamine oxidase inhibitors now in use as antidepressants. More thorough double-blind controlled trials with larger numbers of patients are needed to clarify the action of both procaine and GH3 in the elderly. (Journal abstract modified)

229504 Higuchi, Masamoto; Murakami, Eiji; Goto, Yuichiro; Nakamura, Yasumasa; Nagahama, Fumio; Kawakita, Yasuo; Yamazaki, Tokuji; Iseri, Yoshihisa. Dept. of Internal Medicine, Jikeikai University School of Medicine, Tokyo **The clinical evaluation of a new minor tranquilizer clorazepate dipotassium (Mendon) in the treatment of patients with psychosomatic disease, neuroses and depressive state in a double blind clinical study.** Journal of Japanese Psychosomatic Society (Fukuoka). 15(4):236-250, 1975.

Efficacy, safety and optimum dosage of Mendon (clorazepate dipossium) were studied in a double-blind comparison with diazepam and placebo in 181 patients presenting psychosomatic diseases, neuroses and depressive states. Physicians' judgements of overall therapeutic response showed statistically significant differences in favor of Mendon over placebo but no significant difference when compared to diazepam. In proportion to the period of therapy, Mendon showed a tendency of a rising curve of improvement in symptoms, which was clearer than diazepam according to two

evaluation scales. Laboratory findings and examination of side-effects indicate that Mendon is safe. Results indicate that 9mg of Mendon per day is the optimum effective dosage. However, it is recommended that the dosage be tailored to the need of each patient. 16 references. (Author abstract modified)

229550 Benassi, Piero; Catalano, Alberto; Forino, Vittorio. Istituto Psichiatrico S. Lazzaro, Reggio Emilia, Italy /**Clinical-therapeutic experiments on psychotic patients with long-acting fluphenazine.**/ Esperienze clinico-terapeutiche su pazienti psicotici con "flufenazina ritardo". Rivista di Psichiatria (Roma). 10(1):27-36, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, the effects of long-acting fluphenazine on chronic psychotics, mainly those affected with schizophrenia, were reported. The results obtained suggest that fluphenazine decanoate is preferable to fluphenazine enanthate both for clinical efficacy and for tolerance. Chronic delirious psychoses improved more with fluphenazine decanoate. With respect to the incidence and intensity of side-effects, the inferiority of fluphenazine enanthate is evident. In a consistent percentage of cases treated with fluphenazine enanthate, depression of humoral tonus occurred, necessitating precautions against suicidal behavior. With fluphenazine decanoate, the frequency of dysphoric manifestations and extrapyramidal phenomena was very low. 23 references.

229551 Bertolino, Antonio; La Mura, Giuseppe. Casa della Divina Provvidenza, Ospedale Psichiatrico Bisceglie, Bari, Italy /**Clinical experiments with fluphenazine decanoate in hospitalized patients.**/ Esperienze cliniche con flufenazina decanoato in pazienti ospedalieri. Rivista di Psichiatria (Roma). 10(1):37-43, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, a clinical experiment with fluphenazine decanoate was reported. One hundred six hospitalized psychotics served as Ss; administration was parenteral and dosage varied from a minimum of 12.5mg to a maximum of 50mg. Results were good in 74 patients, moderate in 28, null or negative in 4. Significant effects were noted in patients with psychotic personality structure who had been hospitalized for a long period and were completely detached from reality with regard to a relatively rapid "restructuring" of the personality and better ties to reality. Side-effects were transitory or controllable. Twenty seven patients with good results were discharged from the hospital, and only eight were readmitted.

229560 Sabbatini, Franco. Clinica delle Malattie Nervose e Mentali, Universita degli Studi di Torino, Turin, Italy /**Clinical therapeutic experiments with fluphenazine decanoate in treating dissociative syndromes.**/ Esperienze clinico-terapeutiche con la flufenazina decanoato nel trattamento di sindromi dissociative. Rivista di Psichiatria (Roma). 10(1):111-121, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, clinical therapeutic experiments in treatment dissociative syndromes with fluphenazine decanoate (FD) were reported. Extrapyramidal phenomena appeared in around two thirds of the cases, generally in those Ss who had exhibited such effects in previous treatment with incisive neuroleptic agents. The use of tricyclic antidepressants was necessary in three cases to treat depression. Paranoid forms of illness benefited from the treatment more rapidly and positively, especially cases of recent onset. In the two cases of catatonia, one responded with reduction of aggressive impulses. 24 references.

229626 Kimura, Sada; Miyake, Hideaki. Department of Psychiatry, Kansai Medical University, Osaka, Japan **Clinical experience in using Mendon (dipotassium clorazepate).** Japanese Journal of Clinical Psychiatry (Tokyo). 4(3):340-348, 1975.

The effect of Mendon (dipotassium clorazepate) on neurosis and neurotic symptoms was studied, based on an experiment in which 37 patients with neurosis, and five patients with depression and arteriosclerosis were treated with this drug (7.5-30mg/day) for 1-34 weeks. The drug was effective in the majority of patients, with an effectivity rate of 85.7%. It was primarily effective in relieving insomnia, anxiety and tension, irritation, and hypochondriac complaints. A dose of 7.5mg of Mendon had as strong effect as 3mg of diazepam or 5mg of medazepam, and although it may be inferior in its effect on depression compared to diazepam, it has fewer side-effects. 8 references.

229715 Irvin, C. Warren, Jr.; O'Sheal, Frank E. Columbia, SC **Stress and myocardial infarction.** Journal. 71(9):265-269, 1975.

The relationship between emotional stress and myocardial infarction was evaluated in patients admitted to a coronary care unit, and the amount and role of anxiety during acute and convalescent phases of the illness was assessed. The amelioration of stress symptoms with drugs was studied in a comparative experiment using phenobarbital and Librium (chlordiazepoxide). Results show that emotional stress is a precipitating factor in the onset of myocardial infarction. Use of the Minnesota Multiphasic Personality Inventory (MMPI) failed to demonstrate basic differences in personality patterns from the average. These MMPI results also fail to corroborate findings of an earlier study which show that increased anxiety at the time of admission is followed by decreasing anxiety beginning 6 months after infarction. Results of the drug study show no great clinical difference, and statistical studies reveal no major advantage of one drug over the other. It is concluded that a patient's anxiety about his illness and the coronary care unit could be relieved with a moderate expenditure of time and effort. It is felt that both chemical and emotional supportive care is beneficial under these stressful conditions. 13 references.

229717 Young, Laurens D. Dept. of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC 29401 **The medical-pharmacological management of acute psychoses.** Journal. 71(9):274-281, 1975.

Methods of psychiatric/medical management are described which allow the primary physician to provide prompt, decisive palliative care for the patient who presents in an acute psychotic state until more comprehensive psychiatric care can be arranged. The essentials of recognition and management of psychotic behavior are outlined, and some of the newer, primarily chemical approaches to the treatment of psychotic disorders which can be utilized with some efficacy in a general hospital setting are described. Emphasis is on the critical period of the first 72 hours following admission. Instructions are given for diagnosis, admission to the hospital ward, and rapid sedation with psychoactive drugs (chlorpromazine) and nonsedative drugs (haloperidol). 21 references.

229840 Salzman, Carl; Shader, Richard I.; Harmatz, Jerold; Robertson, Linda. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Psychopharmacologic investigations in elderly volunteers: effect of diazepam in males.** Journal of the American Geriatrics Society. 23(10):451-457, 1975.

The effects of daily doses of 12mg of diazepam administered to elderly male volunteers over a 2 wk period were assessed. Ss were divided into placebo and experimental groups, and a battery of psychological tests were administered on a pretest - posttest basis to measure changes in anxiety state, depression, memory and motor functioning. Differential responses to these compounds partially depended upon age and the initial symptom level. Diazepam produced sedative side-effects, a modest antidepressant effect, and a reduction in memory. Placebo had an antianxiety effect in the relatively older Ss, and was associated with decreased fatigue, improved memory and improved motor function. Considerable variability was observed in both drug and placebo responses among the elderly. 32 references. (Author abstract modified)

229921 Campbell, Magda. Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY **Pharmacotherapy in early infantile autism.** Biological Psychiatry. 10(4):399-423, 1975.

At the symposium on Recent Advances in the Field of Early Infantile Autism, held in Boston in June 1974, as part of the program of the Annual Meeting of the Society of Biological Psychiatry, a current review of drug treatment in psychoses of early childhood was presented. It was noted that experience has shown that a therapeutically effective potent drug can make the autistic child more amenable to other therapies, including special education. Knowledge is lacking about the effect of various psychoactive agents on cognition in this patient population as well as their influence on growth, weight, endocrine systems, and organs. A great need for classification was stressed. It was suggested that clinical distinctions be correlated or even improved by certain biochemical, neuroendocrine, and physiological criteria. 125 references. (AUthor abstract modified)

230002 Mangold, Burkart. Univ.-Kinderklinik, Anichstr. 35, A-6020 Innsbruck, Austria **/Treatment of the minimal brain dysfunction syndrome with psychopharmacotherapy (a clinical study with Captagon)./** Medikamentose Behandlung des Minimal-Brain-Dysfunction-Syndroms (eine klinische Studie mit Captagon). Praxis der Kinderpsychologie und Kinderpsychiatrie (Gottingen). 24(5):185-190, 1975.

Clinical experiences with fenetyllin (Capagon) in treating the minimal brain dysfunction (MBD) syndrome in children are reported, and experimental and clinical studies dealing with the treatment of the MBD syndrome with psychostimulants are reviewed. The criteria for initiating pharmacotherapy in MBD children are carefully considered. 16 references. (Journal abstract modified)

230010 Extein, Irl; Bowers, Malcolm B., Jr. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT **The pharmacologic meaning of successful antipsychotic-antidepressant combinations.** Comprehensive Psychiatry. 16(5):427-434, 1975.

The clinical observation that antipsychotic and antidepressant drugs may exert their respective therapeutic effects independently when used in combination in patients displaying mixed symptomatology is reported, and pharmacological implications are discussed. In light of current pharmacologic concepts, this clinical observation argues that the mechanisms of action of antipsychotic and antidepressant drugs involve different biogenic amines at different anatomic sites. This argument reinforces current data from the laboratory and the clinic suggesting that dopamine systems are crucial to the etiology and therapy of schizophrenic psychoses and that norepinephrine systems are crucial in the etiology and therapy of depression. This observation underlines the value of a two-way interchange between pharmacologically knowledgeable clinicians and clinically astute pharmacologists. 62 references. (Author abstract modified)

230104 McGrath, S. D. St. John of God Hospital, Stillorgan, Co. Dublin, Ireland **A controlled trial of chlormethiazole and chlordiazepoxide in the treatment of the acute withdrawal phase of alcoholism.** British Journal of Addiction (London). 70(Suppl. 1):81-90, 1975.

At a conference on alcoholism, held in Stockholm in September 1974, a double-blind controlled trial of chlormethiazole (Heminevrin) and chlordiazepoxide (Librium), conducted on 97 patients admitted to a specialized unit for the treatment of alcoholism in a psychiatric hospital, was reported. Findings show that both of these drugs were effective in managing the withdrawal phase in the type of alcoholic studied, most of whom had a history of alcohol abuse ranging from 3 to 30 years. Fourteen patients on chlordiazepoxide prematurely stopped treatment in the first 7 days as opposed to seven patients on chlormethiazole, suggesting better control of symptoms by the latter drug. Chlromethiazole showed advantages over chlordiazepoxide in that four cases on the latter drug developed delirium tremens as opposed to none on the former. 4 references.

230368 Stores, Gregory. Dept. of Psychiatry, Univ. of Oxford, Warneford Hospital, Oxford OX3 79JX, England **Behavioral effects of anti-epileptic drugs.** Developmental Medicine and Child Neurology (London). 17(5):647-658, 1975.

The effects of antiepileptic drugs on behavior are discussed. It is noted that: there is increasing evidence that various tupes of behavior disturbances may occur from the use of antiepileptic medication; these disturbances may not always be reversible; there are certain groups of patients, such as those with structural brain damage, who are particularly susceptible. The effects of various antiepileptic drugs are described. It is concluded that the psychopharmacology of antiepileptic drugs is unsatisfactory at present because of inadequate and unsophisticated reporting of behavioral change and because of polypharmacy. It is suggested that more observations are needed on less heterogeneous groups of patients than have been described in the past. 46 references. (Author abstract modified)

230562 Van Putten, Theodore; Sanders, David G. Brentwood VA Hospital, Wilshire & Sawtelle Blvds., Ward 210-C, Los Angeles, CA 90073 **Lithium in treatment failures.** Journal of Nervous and Mental Disease. 161(4):255-264, 1975.

Thirty five patients with chronic and incapacitating mental illness who had not responded to the usual pharmacological and interactional therapies were treated with lithium. None of these patients were diagnosed as suffering from manic-depressive illness. If a trial of lithium resulted in unexpected improvement, lithium's contribution was assessed by double-blind substitution of a placebo followed by lithium in an A-B-A-B design in which the patient served as his own control. Five patients improved dramatically; in retrospect, four of these five patients suffered from nonremitting forms of manic-depressive illness and the fifth patient suffered from a severe obsessive-compulsive neurosis. Six other chronically hospitalized patients improved to the point of unexpected discharge. A trial of lithium therapy is recommended for the intractable patient. 27 references. (Author abstract)

230743 Lal, Samarthji; De La Vega, Charles E. Department of Psychiatry, Queen Mary Veterans' Hospital, Montreal, Quebec **Apomorphine and psychopathology.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(7):722-726, 1975.

In a study of apomorphine and psychpathology, 40 men, mainly alcoholics, were administered either the dopamine receptor agonist, apomorphine HCl, or distilled water subcutaneously three times a day for 14 days in a double-blind study. None of the subjects developed an endogenous depression or schizophrenic symptoms. Scores on the Hamilton Rating Scale, Zung Self Rating Scale, and Brief Psychiatric Rating Scale showed improvement with both apomorphine and placebo. There were no significant differences between the two treatments on these rating scales. A significant incidence of spontaneous penile erections occurred after apomorphine treatment compared with placebo. Both treatments eliminated subjective craving for alcohol. Acute administration of apormorphine had no effect on psychomotor retardation or depressed mood in two patients with endogenous depression. 31 references. (Author abstract)

230991 Atanasio, G.; Bisogni, A. Ospedale Psichiatrico "S. Niccolo", Siena, Italy **/Sulpiride in chronic psychoses of the paranoid type./** La sulpiride nelle psicosi croniche di tipo paranoide. Rassagna di Studi Psichiatrici (Siena). 64(3):446-456, 1975.

The use of sulpiride was investigated for its resocializing effect in treating chronic psychoses of the paranoid type. Fifteen cases of hospitalized paranoid psychotics served as Ss; duration of treatment was on the average 60 days. The results were as follows: three very good results, four good results, four moderate results, and three inadequate results. Even in cases where delirious and chronic hallucinations did not disapper, better coping behavior and better mood tone was obtained. It is suggested that further research be conducted, using sulpiride in the treatment of chronic psychotics who have been hospitalized for long periods of time. 16 references.

230993 Ombrato, M.; Biasci, G. Ospedale Psichiatrico di Volterra, Pisa, Italy **/The "resocializing" effect of clothiapine in chronic psychoses./** Azione "risocializzante" della clotiapina nelle psicosi croniche. Rassegna di Studi Psichiatrici (Siena). 64(3):465-472, 1975.

Clothiapine was investigated for its resocializing effect in treating a group of 22 chronic psychotics. Initial dosage was between 60 and 160mg for a period of from 3-8 weeks; maintenance dosage was between 20mg and 40mg. Results were very good in seven patients, good in 14, and unsatisfactory in one. With respect to schizophrenia, the best results were obtained in the paranoid type. With simple schizophrenia, good results were obtained in the majority of cases. It was noted that clothiapine has a particular sedative effect on aggressiveness, impulsiveness, and anxiety. 20 references.

230997 Ryznar, J.; Uhlir, F. 746 33 Opava, Olomoucka 88, Czechoslovakia **/Cytologic study of cerbrospinal fluid in chronic psychiatric patients treated with neuroleptics./** Cytologicka studie likvoru chronickych psychiatrickych nemocnych lecenych neuroleptiky. Ceskoslovenska Psychiatrie (Praha). 70(2):93-97, 1974.

Sixty six patients suffering from chronic forms of schizophrenia and oligophrenia were subjected to a cytologic evaluation of cerebrospinal fluid in sedimentation chamber. Both groups of patients had monocytic reaction type of fluid cells; changes were more evident in oligophrenics. A subacute irritation syndrome of a general character was also noted. Pleiocytosis was found more often in acute forms of schizophrenia. There was no statistically significant difference in values of differential counts of fluid elements in treated or transiently untreated patients with chronic forms of schizophrenia or oligophrenia. Even high doses of neuroleptic drugs did not substantially affect proportional representation of individual cell types in the same patients both under treatment and when therapy was withheld. 8 references. (Journal abstract modified)

231369 Roccatagliata, G. Clinica delle Malattie Nervose e Mentali, Universita di Genova, Genoa, Italy **/Treatment of Huntington's chorea with trifluoperazine./** Trattamento della corea di Huntington con trifluoperazina. Neuropsichiatrica (Genova). 30(1-2):133-137, 1974.

The results obtained after treating three Ss suffering from Huntington's chorea with high doses of trifluoperazine are reported. Trifluoperazine's blockage of striatal adrenergic receptors causes a depletion of catecholamine and indolamine which is accompanined by improvement in the clinical picture. Two of the Ss were markedly improved after treatment with trifluoperazine, while the third, more seriously afflicted S, improved only moderately; after treatment there was no substantial modification in urinary excretion of catecholamines, 5-hydroxyindolacetic acid, and vanillylmandelic acid. The results confirm the dysmetabolic hypothesis which attributes Huntington's chorea to a hereditary enzymatic error. 6 references.

231654 Chandra, B. Dept. of Neurology, University of Airlangga School of Medicine, Surabaya, Indonesia **Long-term treatment of petit mal with clonazepam.** Modern Medicine of Asia (Hong Kong). 11(7):15-16, 1975.

Long-term treatment of 78 petit mal patients with clonazepam was evaluated in terms of therapeutic results and side-effects. At 1 year followup, attacks had disappeared in 67% of the patients and a substantial reduction of attacks was observed in 14.6%. Four years followup of 14 patients showed absence of attacks in eight subjects and substantial reduction of attacks in three. Side-effects, although not infrequent, were relatively mild. They disappeared when dosage was lowered from 0.2mg/kg to 0.1mg/kg bodyweight. 9 references.

232324 Gillin, J. Christian; Horwitz, David; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, NIMH, Bethesda, MD 20014 **Pharmacologic studies of narcolepsy involving serotonin, acetylcholine, and monoamine oxidase. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 21 p.

The role of serotonergic and cholinergic pathways in the pathophysiology of narcolepsy was evaluated in 13 patients. While the narcoleptic did exhibit differences in their response to parachlorophenylalanine and 5-hydroxytryptophan as compared with nonnarcoleptics who received these drugs, findings do not demonstrate that a pronounced aberration of these neurotransmitter systems is the basis for narcolepsy. Nine patients treated with either phenelzine or pargyline for the management of narcolepsy all showed some symptomatic improvement. However, long-term use of these drugs was precluded by the development of side-effects. 21 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

226936 Bennett, James P., Jr.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Balitmore, MD 21205

Stereospecific binding of d-hysergic acid diethylamide (LSD) to brain membranes: relationship to serotonin receptors. Brain Research (Amsterdam). 94(3):523-544, 1975.

The stereospecific binding of D-lysergic acid diethylamide (LSD) to rat brain membranes is described. D-(3H)LSD binds saturably, reversibly, and with a high affinity to rat brain membranes. Binding is enriched in crude microsomal (P3) membranes. D-(3H)LSD binding is stereospecific as L-LSD, the psychotropically inactive enantiomer, is 1000 times weaker than D-LSD as a displacing agent. The potencies of other LSD analogs parallel their psychotropic activity with the exception of 2-bromo-LSD (psychotropically inactive) which is as potent as D-LSD in displacing bound D-(3H)LSD. Serotonin is the only putative neurotransmitter with affinity for the LSD binding site, and psychotropically active alkylindoleamines are also potent displacing agents. Destruction of presynaptic serotonin neuronal elements by lesioning the midbrain raphe nuclei does not change the affinity or maximum number of detectable in vitro D-(3H)LSD binding sites. Evidence suggests that D-(3H)LSD binds to postsynaptic serotonin receptors. 47 references. (Author abstract modified)

226991 Gorelick, David Alan. Yeshiva University **Facilitation and disruption by mescaline of shuttlebox avoidance in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-17515 HC$13.50 MF$5.00 390 p.

The existence of distinct facilitory and disruptive effects of mescaline in the same strain of animal, in the same conditioning task, and at the same doses was demonstrated, and evidence was gathered as to whether mescaline's two effects have separate mechanisms of action. Changes in behavioral processes which accompany mescaline's effects and the role of stress as a factor in the facilitory effect were assessed, and the influence of decreases in brain catecholamine and serotonin levels on mescaline's two effects were determined in adult, male Long-Evans rats. The question whether mescaline's dual effects are shared by N,N-dimethyltryptamine (DMT), a hallucinogenic indolealkylamine, or 3,4-dimethoxyphenylethylamine hydrochloride (DMPEA), a non-hallucinogenic mescaline analog was investigated. The behavioral system used was discriminated shuttlebox avoidance, and data were collected on the following dependent variables: avoidance rate, number of shuttlebox crossings during a 5 min presession period, number of shuttlebox crossings during the intertrial intervals, and response latency. Results indicate that mescaline does cause distinct facilitory and disruptive effects on avoidance behavior, a property not shared by the two related drugs. (Journal abstract modified)

231480 Gordon, Pearl-Ellen. New York University **The effects of LSD on the expression of affect in psychotherapy (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-22888 HC$13.50 MF$5.00 210 p.

The claims of stimulated emotional growth, intensified abreaction and increased introspectiveness reported in the literature on lysergic acid diethylamide (LSD) as an aid to psychotherapy were investigated, as reflected by various parameters of verbal expression of emotion in seven patients given subhallucinatory doses of LSD as well as active (dextroamphetamine) and inactive (lactose) placebo during several intervals of treatment. Findings which could be generalized were sparse. LSD did result in a significant increase in the experience of witty, carefree, playful emotions. Patients given LSD also spoke significantly more about laughing and crying than in response to placebo drugs. While not satisfying the rigorous conditions for significance, certain trends were noted in reactions to the LSD treatment, although a conclusive statement about the exact role of LSD as an aid to therapy could not be made. (Journal abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

226351 Voiculescu, V.; Pruskauer-Apostol, Beatrice; Alecu, C. Neurological Clinic, G. Marinescu Hospital, Bucharest, Romania **Treatment with acetazolamide of brain-stem and spinal paroxysmal disturbances in multiple sclerosis.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(2):191-193, 1975.

The treatment of brainstem and spinal paraxysmal disturbances in multiple sclerosis with acetazolamide is reported. Nine cases of multiple sclerosis with paraxysmal disorders were treated with acetazolamide. In most cases a brainstem origin of the seizures was suggested by their particular pattern: crossed syndromes (facial spasm associated with contralateral weakness of the arm and leg, paroxysmal paresthesiae in one side of the face and weakness of the contralateral leg), paroxysmal dysarthria, and ataxia. One patient with a Brown-Sequard syndrome complained of paroxysmal paresthesiae in the lower limbs, for which a spinal origin was admitted. In all patients the paroxysmal disorders were promptly suppressed or markedly reduced by acetazolamide. 8 references. (Author abstract modified)

226731 Murphy, Dennis L.; Costa, Jonathan L. Section on Clinical Neuropharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Utilization of cellular studies of neurotransmitter-related enzymes and transport processes in man for the investigation of biological factors in behavioral disorders. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 31 p.

Biogenic amine related characteristics of the platelet are surveyed, and ways in which this model can be utilized in the study of psychoactive drug effects and behavior are illustrated. Studies are reported which suggest that monoamine oxidase (MAO) platelet activity represents a relatively stable genetically influenced characteristic of the individual and may be useful in correlating, or eventually predicting, some other characteristics which may be influenced by familial and genetic factors. This assumption is supported by studies which suggest an increase of octopamine in human platelets in response to MAO inhibition. Findings indicate that it may be possible to monitor individual differences in response to drugs and to correlate these differences with both biological changes and clinical changes in patients' behavior. 75 references.

226737 Van Gelder, N. M.; Sherwin, A. L.; Sacks, C.; Andermann, F. Department de Physiologie, Universite de Montreal, Montreal, Quebec **Biochemical observations following administration of taurine to patients with epilepsy.** Brain Research (Amsterdam). 94(2):297-306, 1975.

Amino acid analysis of plasma and urine obtained from 12 patients with epilepsy is described. Results indicate that the plasma concentrations of taurine and glutamic acid were much higher than might have been expected. Glutamic acid in urine was also increased in these patients. Oral administration of taurine did not appreciably affect the levels of amino acids in plasma or urine with the exception of that of glutamic acid. In patients with an abnormal plasma concentration of glutamic acid, the administration of taurine caused glutamic acid levels to change in the direction of normal values along with a

decrease in the urinary excretion of this amino acid. This action of taurine was independent of either its initial or final plasma concentration. Amino acid concentrations in the cerebrospinal fluid (CSF) were within normal range and were influenced by taurine administration. The selective elevation of both taurine and glutamic acid in the plasma implies that some patients with epilepsy may suffer from an aberration in taurine and glutamic acid metabolism. It is suggested that in future clinical trials investigating the potential use of taurine as an antiepileptic agent, the oral dose of taurine should not exceed 1.0g/day, and optimal doses may be as low as 0.1-0.5g/day. 18 references. (Author abstract modified)

226829 Pond, Susan M.; Graham, Garry G.; Birkett, Donald J.; Wade, Denis N. Department of Clinical Pharmacology, St. Vincent's Hospital, Darlinghurst, Sydney, N.S.W. Australia, 2010 **Effects of tricyclic antidepressants on drug metabolism.** Clinical Pharmacology and Therapeutics. 18(2):191-199, 1975.

The effects of chronic treatment with amitriptyline and nortriptyline on the elimination from plasma of warfarin, dicumarol, phenytoin, and tolbutamide were examined in healthy 20-25-year-old male volunteers. No alteration of plasma half-life of warfarin, phenytoin, or tolbutamide was observed following dosage with the tricyclic antidepressants used. There was no consistent effect on the metabolism of dicumarol following treatment with amitriptyline or nortriptyline although the bioavailability of dicumarol appeared to be increased. In some subjects, this increased bioavailability was associated with significant prolongation of the plasma half-life of dicumarol due to its dose dependent kinetics. 33 references. (Author abstract)

226900 Saarma, J.; Saarma, M.; Aadamsoo, A.; Jatsa, K.; Liivamagi, J.; Mehilane, L. Laboratory of Psychopharmacology, Tartu State University, Tartu, U.S.S.R. **The effect of succinic semialdehyde and sodium succinate on the higher nervous activity in normal subjects.** International Pharmacopsychiatry (Basel). 10(3):149-156, 1975.

In 15 normal volunteers the action of succinic semialdehyde (SSA), and in 24 volunteers the effect of sodium succinate (SS), on the higher nervous activity (HNA) were investigated. Findings indicate that SSA brings about some enhancement of the excitatory process in cortical activities, accompanied by subjective improvement of memory and concentration. The administration of SS improves the stability of cortical excitatory process and its equilibrium with cortical inhibition; and enhances the connecting activity of the verbal system. These changes parallel the subjective elevation of mood and of general tone. It is concluded that succinic acid may be a psychoenergizer. The task of further investigations is to establish the range of therapeutic activity of these compounds. 20 references. (Author abstract)

228310 Hada, Hiro. Department of Psychiatry, Kanto Teishin Hospital, Japan **Recent views in psychopharmacology: its biochemical aspect.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1273-1280, 1974.

Recent research in psychopharmacology is discussed. Research on amine metabolism, the relationship between thyroid function and antidepressants, cyclic adenosine monophosphate, and lithium are considered. 50 references.

228997 Smith, S. E. Department of Pharmacology, St. Thomas's Hospital Medical School, London, England **How drugs act -- 11. Drugs and sleep.** Nursing Times (London). 71(36):1417-1418, 1975.

The action of hypnotic drugs is discussed. It is noted that, while the barbituates are the most effective hypnotic agents, their mode of action is still largely obscure. They produce widespread suppression of activity in the brain, affecting all areas from the cerebral cortex to the medulla. Cortical depression is significant for a number of reasons: it is responsible for the anticonvulsant activity of these drugs; it causes impairment of memory and concentration; and it leads to a reduction of inhibitory activity. Barbiturates are habit forming and cause enzyme induction in the liver; they are often replaced by the benzodiazepines, which depress the reticular formation and induce sleep, but rarely cause habituation. Benzodiazepines depress rapid eye movement sleep, and have mild sedativetranzuilizing and anticonvulsant actions. Other hypnotics include chloral derivatives, glutethimide, and chlormethiazole.

229042 Syvalahti, E. K. G.; Kanto, J. H. Department of Pharmacology, University of Turku, Turku 52, Finland **Serum growth hormone, serum immunoreactive insulin and blood glucose response to oral and intravenous diazepam in man.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):74-82, 1975.

The effect of diazepam on blood glucose, serum immunoreactive insulin (IRI), and growth hormone (GH) was studied in 10 volunteers who received diazepam in oral doses of 5mg or 10mg, or 10mg intravenously. They also received placebo and saline treatment. There was a dose dependent rise in GH after diazepam administration, and the rise was related to the peak plasma level of the drug. A highly significant correlation between the concentrations of serum GH and plasma diazepam was found. Following the intravenous and oral administration of 10mg of diazepam, the peak GH levels at 30 and 60 minutes were significantly higher than those during saline and placebo periods. There was a tendency toward elevation of blood glucose levels, but no significant changes of serum IRI. 43 references. (Author abstract modified)

229115 Roman, I.; Romila, A. Clinica de psihiatrie, I.M.F. Bucharest, Rumania **/An electroencephalographic study of the value of activation by megimid in psychiatric diseases./** Studiul electroencefalografic asupra valorii activarilor cu megimid in bolile psihice. Neurologie, Psihiatrie, Neurochirurgie (Bucuresti). 20(2):103-111, 1975.

The bioelectrical, cerebral and clinical behavior of psychotic patients was investigated during activation with convulsant substances of the megimid type (beta-ethyl, beta-methylglutharimide). Tracings were altered after activation in 39.1% of the cases; most cases did not exhibit a reaction. The following aspects were investigated in more detail: irritative nonspecific abnormalities; lesional abnormalities due to sequellae not known before activation; the convulsant threshold, expressed through the smallest amount of megimid that determined the first paroxystic complexes of spike waves; convulsions induced by activation. Altered convulsant thresholds and induction of convulsions were noted during pharmacodynamic activation in some patients with nonepileptic psychic disturbances; this necessitates a more critical attitude in the electroclinical correlations of results obtained by drug activation. 23 references. (Journal abstract modified)

229471 Wheatley, David. Research Group, Twickenham, Great Britain **Psychopharmacology of the circulatory system.** Psychopharmacology Bulletin. 11(4):64-66, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974, a study of the psychopharmacology of the circulatory system was reported,

which focused on four aspects: (1) the relationship between stress and ischemic heart disease and the control of anxiety with beta adrenergic blocking drugs; (2) the cardiotoxic effects of psychotropic drugs considered from the experimental and clinical viewpoints; (3) anxiety and hypertension (anxiety induced hypertension in the laboratory and use of antianxiety drugs in treating hypertension); and (4) psychogeriatrics (the effects of psychotropic drugs on the electroencephalogram of elderly Ss and relief of psychiatric symptoms by peripheral vasodilator drugs). Results of animal and clinical studies as related to the use of psychotropic drugs that affect the circulatory system in these areas were reported. 7 references. (Journal abstract modified)

229473 Itil, Turan M.; Akpinar, S.; Herrmann, W. New York Medical Center, Department of Psychiatry, New York, NY **Discovery of "specific" CNS effects of lisuride hydrogen maleate -- an antimigraine compound.** Psychopharmacology Bulletin. 11(4):67, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974, a study of the central effects of lisuride hydrogen maleate (LHM), a new antimigraine compound similar to methysergide, was reported. Based on computerized electroencephalograms, it was concluded that LHM has sytematic effects on human brain function with some similarities to psychostimulant compounds and anxiolytic drugs. Pilot clinical trials suggested certain therapeutic effects in acute and chronic brain syndrome Ss, as well as in behaviorally disturbed hyperkinetic children and geriatric patients. Subsequent animal trials also demonstrated that LHM has stimulatory effects, along with some central nervous system (CNS) depressive action on mice; direct stimulatory effects of dopamine receptors also occurred. According to animal pharmacology, LHM may represent a new group of compounds with potent effects on both serotonergic and dopaminergic systems. The search for the clinical therapeutic usefulness of LHM is underway. (Journal abstract modified)

229492 Rivera-Calimlim, Leonor. University of Rochester School of Medicine and Dentistry, Rochester, NY **Plasma chlorpromazine in psychiatric management.** Psychopharmacology Bulletin. 11(4):76-77, 1975.

The significance of chlorpromazine (CPZ) plasma levels in psychiatric patients receiving CPZ and other forms of therapy is being investigated. The plasma CPZ levels of 50 acutely psychotic inpatients have been measured by gas/liquid chromatography, and the clinical progress of 29 acute patients has been monitored by the Brief Psychiatric Rating Scale once a week for 4-6 weeks. CPZ plasma levels of 50-300ng/ml were generally associated with clinical improvement, especially in paranoid behavior and thought disorder. This range was best attained by doses of 400-800mg/day. A single dose of 400-800mg at bedtime produced steady states of plasma CPZ equal to or better than those achieved by a multiple dosage schedule of the same total daily dose in the same patients. Trihexyphenidyl (Artane) a commonly used antiparkinsonian agent, decreased plasma CPZ significantly. The interaction appeared to be in the absorption stage. Ss who did not attain adequate plasma CPZ levels despite 400-1000mg/day doses were receiving lithium throughout the study period, with a diagnosis of manic-depressive (manic) and schizoaffective (excited). The lithium and CPZ interaction is currently being studied. (Journal abstract modified)

229826 Fischbach, R. Landesnervenklinik Salzburg, Neurologische Abteilung, A-5020 Salzburg, Ignaz-Harrer-Str. 79, Austria **/Changes in imipramine induced noradrenaline potentiation by varying activity of gastric juice under oral medication./** Veranderungen der durch Imipramin bedingten Noradrenalinpotenzierung durch unterschiedliche Magensaurewerte bei oraler Medikation. Arzneimittel-Forschung (Aulendorf). 25(1):123-131, 1975.

The inhibition of imipramine absorption by decreasing the acidity of gastric juice was studied. From serial studies on imipramine dependent noradrenaline rise at different values of gastric acid with 336 registrations of blood pressure, a dependent relationship was found to exist between imipramine absorption and gastric juice acidity. At pH values of 3.5-6.0, a distinct decreased absorption of orally supplied imipramine was noted. After changing the pH value by acid substitution, a full absorption was reached. Special implications of these findings for the treatment of depression with thymoleptics are discussed. 14 references. (Journal abstract)

230602 Clement-Cormier, Yvonne C.; Kebabian, John W.; Petzold, Gary L.; Greengard, Paul. Department of Pharmacology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Dopamine-sensitive adenylate cyclase in mammalian brain: a possible site of action of antipsychotic drugs.** Proceedings of the National Academy of Sciences. 71(4):1113-1117, 1974.

The hypotheses that the antipsychotic drugs achieve their therapeutic effects by virtue of blocking dopamine receptors in the brain and that a hyperactivity of dopaminergic pathways in the brain is involved in the pathophysiology of schizophrenia were tested in tissues from man and other mammals. Both hypotheses received some experimental confirmation. Adenylate cyclase, selectively stimulated by low concentrations of dopamine, was found in the olfactory tubercle, the nucleus accumbens, and the caudate nucleus of several mammalian species. Several different classes of drugs effective in the treatment of schizophrenia were potent inhibitors of the stimulation by dopamine of the enzyme from these various regions. The inhibition by these antipsychotic drugs was competitive with respect to dopamine. For each of several drugs tested, the Ki for the enzyme from the olfactory tubercle was similar to that for the enzyme from the caudate nucleus. 19 references. (Author abstract modified)

230739 Starling, Lindsey M.; Boullin, D. J.; Grahame-Smith, D. G.; Adams, C. B. T.; Gye, R. S. M.R.C. Unit, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, England **Responses of isolated human basilar arteries to 5-hyroxytrypamine, noradrenaline, serum, platelets, and erythrocytes.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(7):650-656, 1975.

The response of the isolated human basilar artery suspended in Krebs' solution to 5-hydroxytryptamine (5-HT), noradrenaline, and histamine, which stimulate specific receptors was examined. The artery contracted in response to all three drugs. Normal human serum contains an unidentified contractile substance, and erythrocytes relax the artery. Serum and erythrocytes potentiate 5-HT contractions. This preparation is suitable for studying vasoactive substances released during vasospasm after subarachnoid hemorrhage. 14 references. (Author abstract modified)

230763 McLarty, Donald G.; O'Boyle, James H.; Spencer, Carole A.; Ratcliffe, John G. Dept. of Materia Medica, Stobhill General Hospital, Glasgow G21 3UW, Scotland **Effect of lithium on hypothalamic-pituitary-thyroid function in patients with affective disorders.** British Medical Journal (London). No. 5984:623-626, 1975.

Hypothalamic-pituitary-thyroid (HPT) function was assessed in 17 patients on maintenance doses of lithium carbonate (LC) for a mean period of 21 months and by serial studies on four patients from the start of LC treatment for up to 6 months. An exaggerated thyrotrophin (TSH) response to i.v. thyrotrophin releasing hormone (TRH) occurred in 14 out of 17 patients on maintenance treatment, though basal levels were raised in only three. There were no significant differences in thyroid hormone or basal TSH levels between the euthyroid lithium treated patients and a group of controls. In all four patients studied serially an exaggerated TSH response to TRH developed soon after starting LC and persisted throughout the observation period. Basal TSH levels increased in two of the four patients within the first 2 weeks of treatment but no consistent trend was found in total thyroxine and total triiodothyronine levels. It is suggested that the exaggerated TSH response to TRH is due mainly to the well established direct effects of LC on the thyroid. 24 references. (Author abstract modified)

231318 Spiker, Duane G.; Weiss, Alan N.; Chang, Sidney S.; Ruwitch, Joseph F.; Biggs, John T. Western Psychiatric Institute, University of Pittsburgh, Pittsburgh, PA 15213 **Tricyclic antidepressant overdose: clinical presentation and plasma levels.** Clinical Pharmacology and Therapeutics. 18(5 part 1):539-546, 1975.

Fifteen patients were studied at 8 to 12 hour intervals during the first 24 hours after overdosing with tricyclic antidepressants, and subsequently followed daily for up to 144 hours. The severity of the overdose was determined by measuring the plasma tricyclic antidepressant level using gas chromatography/mass fragmentography. No correlation was found between total, tertiary, or desmethyl tricyclic antidepressant plasma levels and maximum heartrate, lowest blood pressure, degree of unconsciousness, or electrocardiogram changes involving the P-R interval or ST-T wave changes. There was a weak correlation between drug plasma level and maximum pupil size and a strong correlation between the duration of the QRS complex and tricyclic antidepressant plasma level. As the total plasma tricyclic level fell, the duration of the QRS interval returned to normal. Thus, the duration of the QRS complex on the electrocardiogram appears to be the most reliable clinical sign for evaluating the seriousness of tricyclic antidepressant overdosage. 21 references. (Author abstract modified)

231319 Griffith, John D.; Nutt, John G.; Jasinski, Donald R. Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **A comparison of fenfluramine and amphetamine in man.** Clinical Pharmacology and Therapeutics. 18(5, part 1):563-570, 1975.

dl-Fenfluramine hydrochloride, d-amphetamine sulfate, and placebo were compared in eight postaddict volunteers, each dose given orally in random sequence at weekly intervals using a double-blind crossover design. Fenfluramine had little effect on blood pressure and temperature but caused a marked dilation of pupils, whereas amphetamine was a potent vasopressor and a weak mydriatic. While fenfluramine produced euphoria in some subjects, its overall effects were unpleasant, sedative, and qualitatively different from amphetamine. Three subjects given 240 mg of fenfluramine experienced brief but vivid hallucinogenic episodes characterized by olfactory, visual, and somatic hallucinations, abrupt, polar changes in mood, time distortion, fleeting paranoia, and sexual ideation. These observations indicate that fenfluramine is a hallucinogenic agent with a pharmacologic profile in man that is not amphetamine like. 23 references. (Author abstract)

232503 Scherberger, R. R.; Kaess, H.; Bruckner, S. Heidelberg 1, Zechnerweg 3, Germany /**Studies on the action of an anticholinergic in combination with a tranquilizer on gastric juice secretion in man.**/ Untersuchungen uber die Wirkung eines Anticholinergikums in Verbindung mit einem Tranquilizer auf die Magensaftsekretion beim Menschen. Arzneimittel-Forschung (Aulendorf). 25(9):1460-1463, 1975.

A double-blind study with intra-individual comparisons was carried out to investigate the effects of 15 mg of (8r)-3alpha-hydroxy-8- isopropyl-1alphaH, 5alphaH-tropanium bromide(plus or minus)- tropate (Sch 1000), 15mg Sch 1000 plus 10mg oxazepam, 10mg oxazepam and placebo with oral administration in randomized sequence on gastric juice volume, amount of acid, concentration and pH values in 12 healthy volunteers. Results show that Sch 1000 and Sch 1000 plus oxazepam were equal in effect on basal and stimulated secretion volume. As compared with placebo, it was not possible to establish an effect on secretion volume for oxazepam alone. Sch 1000 and Sch 1000 plus oxazepam were found to be equipotent in reducing the amount of basal acid, while oxazepam reduced this quantity only during the first 30 min of basal secretion. None of the three active preparations was capable of inhibiting the stimulated acid, although both Sch 1000 preparations produced a clear trend towards lowered mean values. During the basal secretion period, all three test preparations had an inhibiting action on acid concentration, but none of them had a significant effect during the stimulation period. The pH value was safely increased only by Sch 1000 and Sch 1000 plus oxazepam, and this even only during the basal period. 7 references. (Author abstract)

232520 Cobby, J. M.; Ashford, J. R. Grassland Research Institute, Hurley, Berkshire, England **Drug interactions: the effects of alcohol and meprobamate applied singly and jointly in human subjects. IV. The concentrations of alcohol and meprobamate in the blood.** Journal of Studies on Alcohol. Supplement No. 7:162-176, 1975.

The absorption and elimination of alcohol and meprobamate from the blood during Experiments 4 (E-4) and 5 (E-5) of Carpenter et al. were studied by means of mathematical models representing the relation between doses, concentration in the blood and time elapsing since drug ingestion. The blood concentrations of samples taken 2 and 5.5hr after beginning to drink in E-4, and 1, 1.5, 2, 2.5, 3.5and 4.5hr in E-5 were analyzed. The presence of meprobamate did not affect blood alcohol concentration (BAC) in either experiment. The calculated elimination rate of the two highest doses of alcohol are reported. The blood meprobamate concentrations (BMC) in E-4 were not affected by alcohol. In E-5, 2.5and 5.5hr after meprobamate administration, the combination of 28mg of meprobamate per kg and 0.75g of alcohol per kg resulted in significantly lower BMC than after the same dose of meprobamate with the other doses of alcohol. The differences between these results and the findings of Carpenter et al. are discussed. 5 references. (Author abstract modified)

232531 Korttila, Karl. Dept. of Pharmacology, Siltavuorenpenger 10 A, SF-00170 Helsinki 17, Finland **The effect of diazepam, flunitrazepam and droperidol with an analgesic on blood pressure and heart rate in man.** Arzneimittel-Forschung (Aulendorf). 25(8):1303-1306, 1975.

The effects of i.v. diazepam, droperidol and a new benzodiazepine, 5-(alpha-fluorophenyl)-1,3-dihdro-1-methyl-7-nitro-2H-1,4-benzodiazepi -2-one (flunitrazepam, Ro-5-4200) on blood pressure and heartrate were studied in 62 healthy volunteer students. Observations were made after each drug alone,

after diazepam and flunitrazepam each combined with pethidine, and after droperidol combined with fentanyl. The blood pressure was measured by ausculation and the heartrate by counting the radial pulse. The systolic and diastolic blood pressure was regularly decreased. Changes in the heartrate were slight. Flunitrazepam did not have greater effects than diazepam or droperidol, although the combination of flunitrazepam and pethidine seemed to induce a greater fall in systolic blood pressure than did the combination of diazepam and pethidine. None of the changes observed were clinically significant. 21 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

225783 Millichap, J. Gordon. Northwestern University Medical School, Chicago, IL **Drugs in the management of learning and behavior disorders in school children.** Illinois Medical Journal. 145(4):322-323, 1974.

A discussion of drugs used in the management of learning and behavior disorders in school children is presented, including: methylphenidate, amphetamine sulfate, deanol acetamidobenzoate, chlordiazepoxide, chlorpromazine, reserpine, thioridazine, hydroxyzine hydrochloride, meprobamate, fluphenazine hydrochloride, chlorproxthixene hydrochloride, promazine hydrochloride, phenobarbital, primidone, and diphenylhydantoin sodium. These drugs are used variously to affect hyperactivity (hyperkinesis), emotional disturbances, minimal brain dysfunction, anxiety, and convulsions. The dosage and use of methylphenidate is described in detail. Stimulant medications are recommended as adjuncts to remedial education and as facilitative of a child's abilities to focus on meaningful stimuli and to organize body movements. Lack of proven association between stimulant use and drug abuse is stressed. 5 references.

226069 Rie, Herbert E. Department of Pediatrics, Ohio State University, Children's Hospital, Columbus, OH 43205 **Hyperactivity in children.** American Journal of Diseases of Children. 129(7):783-789, 1975.

Various childhood problems that are often subsumed under the heading of hyperactivity are discussed as to causes, combinations, and detection. The designation does not define a homogeneous group of children, does not consistently point to a common cause, and has treatment implications only in the sense that multiple simultaneous approaches must typically be considered. Stimulant drugs frequently used for control of so called hyperactivity are considered an inadequate treatment when used alone because they have a number of poorly studied effects, some of which are apparently negative and because they may obscure problems other than the hyperactivity itself, which then may be ignored. Evidence now available is used to show that classroom learning does not improve with drug treatment despite common assumptions to the contrary. 40 references. (Journal abstract modified)

226349 Pilling, J. B.; Baker, Janet; Iversen, L. L.; Iversen, S. D.; Robbins, T. Department of Neurology, St. Bartholomew's Hospital, London EC1, England **Plasma concentrations of L-dopa and 3-methoxydopa and improvement in clinical ratings and motor performance in patients with Parkinsonism treated with L-dopa alone or in combination with amantadine.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(2):129-135, 1975.

Plasma concentrations of L-dopa and 3-methoxydopa and improvement in clinical ratings and motor performance were studied in patients with Parkinsonism treated with L-dopa alone or in combination with amantadine. Six patients with idiopathic Parkinsonism were treated with a combination of amantadine and L-dopa and after 12 to 24 weeks amantadine was replaced by placebo for a 6 week period in a double-blind trial. Although there was a tendency for clinical disability ratings and scores on objective ratings of motor skills to deteriorate initially after amantadine removal, there was no significant deterioration found in clinical improvement or motor performance during the period of amantadine withdrawal. Amantadine withdrawal failed to cause any significant change in plasma concentrations of L-dopa or its metabolite 3-methoxy-dopa in these patients. In a group of 27 patients seen regularly as outpatients, measurements of plasma L-dopa failed to correlate significantly with either oral dose or with clinical improvement scores. The plasma concentration of 3-methoxy-dopa, however, was found to be on average 2.8times higher than that of L-dopa, and there was a significant correlation between plasma levels of this metabolite and clinical improvement. It is suggested that 3-methoxy-dopa may contribute significantly to the therapeutic actions of L-dopa in Parkinsonism. 15 references. (Author abstract modified)

226901 Kurland, Albert A.; McCabe, Lee; Hanlon, Thomas E. Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228 **Contingent naloxone (N-allylnoroxymorphone) treatment of the paroled narcotic addict.** International Pharmacopsychiatry (Basel). 10(3):157-168, 1975.

Results are reported of pilot and controlled research on the effectiveness of the contingent (upon narcotic drug use) administration of the narcotic antagonist, naloxone (N-allylnoroxymorphone) to paroled narcotic addicts enrolled in a urine monitoring program conducted in a metropolitan based outpatient clinic. Criteria of effectiveness, which include clinic attendance, the extent of narcotic drug usage, and disposition at the end of a 6 month treatment period, are viewed in relation to already established baseline results with a sample of patients processed through the same clinic over a 5 year period prior to the introduction of naloxone treatment. The pilot study indicated longer patient involvement and less reinstitutionalization than baseline values, but the results of the controlled evaluation reveal no benefit from contingently administered naloxone beyond placebo reactivity. Results are discussed in terms of given sample characteristics, and suggestions are offered regarding the development of new narcotic antagonist treatment approaches. 15 references. (Author abstract modified)

226903 Milstein, Stephen L.; MacCannell, Keith; Karr, Gerry; Clark, Stewart. INRS-Sante, Hopital St-Jean-de-Dieu, Montreal H1N 1ZO, Quebec **Marijuana-produced changes in pain tolerance. Experienced and non-experienced subjects.** International Pharmacopsychiatry (Basel). 10(3):177-182, 1975.

The effects of marihuana and placebo on pain tolerance were compared in cannabis experienced and naive subjects. A statistically significant increase in tolerance was observed after smoking marihuana. Although there was no statistically significant interaction between the drug effect and having had previous cannabis experience, there was a definite trend toward a greater increase in tolerance for the experienced (16%) compared to the naive group (8%). 8 references. (Author abstract)

227140 Risberg, Ann-Marie; Henricson, Sigrid; Elmqvist, Dan; Ingvar, David H. Department of Clinical Neurophysiology, University Hospital, S-221 85 Lund, 5, Sweden **Effects of a new butryophenone derivate (Buronil) on noctural sleep in normal man.** Psychopharmacologia (Berlin). 43(1):95-99, 1975.

Nocturnal sleep was studied in eight young normal volunteers with polygraphic technique during two periods of 10 nights each. After two adaptation and two baseline nights with placebo, they were given methylperone 10 or 50mg per night during three nights and then again placebo for three withdrawal nights. The study was made double-blind. No changes of sleep stages were seen during the drug periods. The lower dose gave an increase of sleep latency but a decrease of number of awakenings during the night. An increase of rapid eye movement (REM) periods was shown after 50mg and also a decrease of REM latency and REM density. The only significant change during withdrawal periods was a decrease of REM sleep after methylperone 50mg, so there was no barbiturate type of withdrawal. The change was also different from that of chlorpromazine, which has no clear rebound effect. 23 references. (Author abstract modified)

227569 Kochansky, Gerald E.; Salzman, Carl; Shader, Richard I.; Harmatz, Jerold S.; Ogeltree, Ann M. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **The differential effects of chlordiazepoxide and oxazepam on hostility in a small group setting.** American Journal of Psychiatry. 132(8):861-863, 1975.

The effects of chlordiazepoxide, oxazepam, and placebo on hostility, as an inner motivational or arousal state, were compared in moderately and highly anxious male research volunteers in a small group setting. The data support the hypothesis that chlordiazepoxide induced increases in motivational hostility are more frequent and intense than those associated with placebo and oxazepam. The data also suggest that oxazepam may be a more specific "hostility tranquilizer" than other benzodiazepines. 18 references. (Journal abstract modified)

227772 Gunby, Bjorn. Dikemark Hospital, N-1385, Solberg, Norway **Clinical physiognomy of flupentixol.** Acta Psychiatrica Belgica (Bruxelles). 74(5):500-506, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the use of flupentixol in the treatment of psychiatric patients was reported. In low doses flupentixol can be used to alleviate anxiety, depression, lack of initiative, and inactivity; in moderate doses it is used in cases involving delusions, hallucinations, and psychotic confusion; and in high doses it is used in cases involving autism, psychotic symptoms, and mania. The results of studies indicate that flupentixol has a rapid onset of action, few or no side-effects, and leaves no drug dependence or withdrawal symptoms.

227820 Ban, T. A.; Lehmann, H. E.; Sterlin, C.; Climan, M. no address **Comprehensive clinical studies with thiothixene.** Diseases of the Nervous System. 36(9):473-477, 1975.

A comprehensive clinical study of thiothixene (TT) was conducted in two phases. The first phase was designed to study the range of therapeutic activity of TT in 60 hospitalized psychiatric patients belonging to four different diagnostic groups. It was found that TT, 4-40mgs/day, produced significant improvement on a number of measures of affect in the psychoneurotic and schizophrenic groups. Some signs of clinical improvement were noted in 10 of 20 psychogeriatric patients. A linear relationship between dosage and adverse effects was noted. The second phase was designed to establish the place of TT among various antipsychotic drugs in 90 hospitalized schizophrenic patients. It was found that TT produced significant changes in the factor scores Social Interest, Personal Neatness and Retardation of the Nurses' Observation Scale for Inpatient Evaluation (NOSIE). Clopenthixol improved factor scores Social Competence, Social Interest, Irritability, Manifest Psychosis and Retardation of the NOSIE, while chlorprothixene improved the Personal Neatness score of the NOSIE. Thiothixene produced the lowest number of adverse effects of the drugs tested. 9 references. (Author abstract modified)

228094 Hug, R. Institut Marcel Riviere, 78320 Le Mesnil-Saint-Denis, France **Hypnotics and sleep: classification, metabolism, mechanism of action of hypnotics and alterations of phases of sleep by hypnotics.** Les hypnotiques et le sommeil: classification, metabolisme, mode d'action des hypnotiques, alteration des phases du sommeil par les hypnotiques. Perspectives Psychiatriques (Paris). 2(51):107-112, 1975.

The classification, metabolism, mechanism of action of hypnotic drugs and the alterations of sleep phases they cause are reviewed. Hypnotic preparations are classified as: vegetable and mineral derivatives; barbiturates (pentothal, nembutal, etc.); nonbarbituric chemical derivatives (alcohols, aldehydes, chloral hydrate, quinazolones, benzodiazepines; and a number of psycholeptics used in small doses (antihistamines, mepronizine). It is noted that most hypnotics act particularly on stage IV sleep and on paradoxical sleep. Any hypnotic taken regularly, every night, causes addiction with major alterations in the quality of sleep. It is felt that present hypnotic preparations should be prescribed with great care because they only mask the true problems which disturb sleep. The physician should attempt to discover the underlying problem before prescribing sleeping preparations. 12 references.

228420 King, Sharon M. Brigham Young University **State-dependent learning in retardates using thioridazine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-19840 HC$13.50 MF$5.00 74 p.

The phenomenon of state-dependent learning was examined in mentally retarded Ss divided into four groups: thioridazine (learning)/thioridazine (recall I)/thioridazine (recall II); thioridazine/placebo/thioridazine, placebo/thioridazine/placebo, or placebo/placebo/placebo. Ss then learned a recognition and short-term memory task to a criterion of perfect retention on two successive occasions. Ss receiving thioridazine were administered 2mg/kg daily divided into two equal doses. It was hypothesized: that Ss experiencing a change in drug condition between the learning and recall I situation which occurred 2 days later would show a definite decline in recall as opposed to Ss remaining in the same drug state in both conditions; that Ss would learn significantly more slowly under thioridazine; and that recall II scores would improve in groups experiencing a drug change in the recall I situation when the original drug condition was reinstated in the recall II situation. Results fail to substantiate any of the hypotheses. (Journal abstract modified)

229081 Dugas, M.; Gueriot, C.; Frohwirth, Ch. Hopital Herold, 7, place Rhin-et-Danube, F 75935 Paris Cedex 19, France **/Is lithium useful in child psychiatry?/ Le lithium a-t-il un interet en psychiatrie chez l'enfant?** Revue de Neuropsychiatrie Infantile etc. (Paris). 23(5-6):365-372, 1975.

Forty three children from 5 to 21 years of age were treated with lithium carbonate. The dosage was calculated with respect to the level of lithium in the blood. It was independent of the weight and age of the S and was generally close to the adult dose. Side-effects were unusual if the blood lithium level was regularly controlled, but digestive disturbances, tremor, and thirst did occur. In general, the side-effects did not involve halting treatment and they disappeared after a few

weeks. The best results were obtained with cases of manic-depressive illness. The results were minimal in cases of psychomotor instability without thymic involvement. The effect was always incomplete with cases of infantile hypomania. It was difficult to evaluate the drug's effect with thymic disturbances occuring in the course of other disorders (schizophrenia, prepsychotic states, etc.). 3 references. (Author abstract modified)

229113 Procopiu-Constantinescu, Thea. Policlinica "Dr. I. Cantacuzino", Bucharest, Rumania **/Attempts at a neurochemical interpretation of natural behavior and behavior modified by neuroleptic drugs./** Incercari de interpretare neurochimica a comportamentului natural si modificat prin neuroleptice. Neurologie, Psihiatrie, Neurochirurgie (Bucuresti). 20(2):81-88, 1975.

An attempt is made to formulate a neurochemical interpretation of normal behavior and behavior modified by neuroleptic drugs. The mechanisms of the following agents are reviewed: phenothiazine, reserpine, chlorprothixene, haloperidol, propandiol, benzothiazepine, monoamine oxidase inhibitors, amphetamines. 37 references.

229128 Bruynooghe, F.; Tanghe, A. J. Social Psychiatry Office, R. U. Groningen, The Netherlands **/Piracetam in a case of acute cerebral hypoxemia: casuistic report./** Piracetam bij acuut hypoxemisch hersenlijden: casuistische mededeling. Tijdschrift voor Psychiatrie (Meppel). 16(10):592-595, 1974.

The positive effect of piracetam in a 57-year-old man with acute cerebral hypoxemia is described. The patient was admitted with melancholia induced by reserpine. His neurological and internal conditions were normal, and he improved rapidly on anafranil injections. Then the patient choked on food, became unconscious, and his air passages were obstructed, resulting in cyanosis, complete areflexia, no spontaneous breathing, no pulse, fecal and urine losses. Four hours later he was in deep coma, with only the corneal reflex and extension cramps present. Within 72 hours both the clinical and electroencephalographic neurological conditions improved when he was given piracetam 1g/hr, corticosteroids, diazepam, and cedelanide. Comparison of the severe clinical and electroencephalographic picture with the subsequent rapid improvement supports the hypothesized contributing effect of piracetam. (Author abstract modified)

229440 Smith, Robert C.; Dekirmenjian, H.; Davis, John M. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Blood level, mood, and MHPG responses to diazepam in man.** Psychopharmacology Bulletin. 11(4):21-23, 1975.

AT the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 a study of the effects of oral doses of diazepam on mood and urinary 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) responses in man was reported. These responses were related to plasma and red blood cell (RBC) levels of the drug over a 6 hr time course using normal volunteers, anxious outpatients, and hospitalized psychiatric patients. The preliminary findings regarding the effects of the diazepam on catecholamine turnover in man contrast with the decrease in norepinephrine turnover reported in biochemical studies with rat brain. These differences may be due to many factors, including sex of Ss, dose, peripheral versus central norepinephrine metabolism, and species differences. 9 references. (Journal abstract modified)

229470 Itil, Turan M. New York Medical Center, Department of Psychiatry, New York, NY **Psychotropic action of sex hormones.** Psychopharmacology Bulletin. 11(4):64, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974, a study of the psychotropic action of sex hormones was reported, focusing on mesterolone, a newly developed androgen, and cyproterone acetate, an antiandrogen. It was predicted that an antidepressant property of mesterolone similar to amino inhibiting antidepressants and stimulant tricyclic antidepressants would be found. The therapeutic effects in depressed patients were quick and dramatic in some cases, while in others, few or no effects were noticed. Computer electroencephalogram profiles of cyproterone acetate showed similarities to those of benzodiazepine anxiolytics, and it was speculated that this compound has antianxiety properties. Open, uncontrolled pilot trials in male Ss with anxiety and in female Ss with premenstrual anxiety depression states suggest that it has such effects in some patients. However, as antianxiety effects occur only in dosages which reduce male sexual activity and interfere with the female menstrual cycle, clinical use is not possible. 6 references. (Journal abstract modified)

229529 Ancona, L.; Saraceni, C.; Cagossi, M. Istituto di Psicologia, Facolta di Medicina e Chirurgia, Universita Cattolica del Sacro Cuore, Rome **/The disinhibiting effect of N (1-ethyl-2-pyrrolidinyl-methyl)2-methoxy-5-sulfamido-benzami ide (sulpiride). 00.** L'effetto disinibente della N (1.etil-2.pirrolidinil-metil-)2.metossi-5.sulfamido-benzamid de (sulpiride). II. Archivio di Psicologia Neurologia e Psichiatria (Milano). 36(1):16-24, 1975.

The disinhibiting effect of sulpiride was investigated in 20 Ss with a high rigidity level. The results indicate that the administration of sulpiride shortened the perception time of changing a cube into a parallelepiped. The results are interpreted according to Broadbent's "filter theory" (1958). In disinhibited Ss, the filter acts according to the requirements of changing reality while inhibited Ss have difficulties in discriminating the value or biological suitability of the incoming information and thus the filter is programmed for a wavelength which changes with difficulty. The disinhibiting drug has an effect on the filter, allowing a more fluid exchange of incoming data. It is hypothesized that the drug's effect in acting on the "exchange" filter of inhibition requires a certain period of time to attain optimum intensity, perhaps because this level of action is deeper. 8 references.

229557 Gambi, Domenico; Bergonzi, Paolo; Pinto, Francesco; Vacchini, Fabio. Clinica delle Malattie Nervose e Mentali, Universita Cattolica del Sacro Cuore, Rome **/Organization of sleep phases in subjects treated with fluphenazine decanoate./** Organizzazione delle fasi di sonno in soggetti trattati con flufenazina decanoato. Rivista di Psichiatria (Roma). 10(1):84-91, 1975.

At the First National Symposium on long-acting Fluphenazine, held in Rome in October 1974, a polygraphic investigation of sleep phases in patients treated with fluphenazine decanoate was reported. Ss were six patients with a schizophrenic type of symptomatology, from 25-56 years of age. The Ss exhibited a progressive increase in total sleep and in rapid eye movement (REM) sleep. The latency of the first REM phase was decreased in the nights following administration of the drug. The low doses used (12.5-25mg i.m.)indicate that fluphenazine hydrochloride and fluphenazine decanoate act on the reticular systems which have been hypothesized to regulate the sleep waking cycle. It is suggested that the changes in the sleep phases could be related to dissociative and hallucinatory symptomatology. 9 references.

229650 Howard, Mark L.; Hogan, Terrence P.; Wright, Morgan W. Dept. of Psychology and Psychological Service Centre, University of Manitoba, Winnipeg 19, Manitoba, Canada **The effects of drugs on psychiatric patients' performance on the Halstead-Reitan neuropsychological test battery.** Journal of Nervous and Mental Disease. 161(3):166-171, 1975.

The relationship between the type and amount of psychotropic drug ingestion was evaluated for 184 psychiatric patients using a complex battery of cognitive/sensory/motor tests (the Halstead-Reitan test battery). The total patients' group included 68 psychotic patients who were being treated with either phenothiazines or other drugs, and 80 neurotically depressed patients who were taking either no drugs, phenothiazines, minor tranquilizers, tricyclic antidepressants, or sedatives. Little effect was noted in terms of psychological test performance when individual drug types were combined and considered in terms of dosage. Upon a more specific analysis of the data, a suggestive trend toward improved performance in the psychotic group and impaired performance in the depressed group emerged. Because this and other suggestive trends were a result of secondary analysis, further analysis is recommended in order to delineate the variables involved. 19 references. (Author abstract modified)

229684 Zawadzki, Zygmunt. Klinika Neurologiczna AM, Kopcinskiego 22, 90-153 Lodz, Poland **/Psychological test investigations of patients treated with carbamazepine for nocturnal enuresis and tics./** Testowe badania psychologiczne u chorych leczonych karbamazepina z powodu mimowolnego moczenia nocnego i tikow. Neurologia i Neurochirurgia Polska (Warszawa). 8(3):461-463, 1974.

Fifty children of both sexes ranging in age from 7 to 15 years were given carbamazepine for the management of nocturnal enuresis and tics and were simultaneously observed for level of intellectual functioning and manifestations of learning processes. The set of psychological tests administered to the children is presented together with the individual results obtained. The favorable effect of the drug on the integration of mental processes is noted. 13 references.

229725 Hirai, Tomio; Kakita, Yasuhide; Shimada, Akinori; Kitamura, Sachiko. Tokyo University Branch Hospital, Department of Neurology, Japan **An electroencephalographic study on psychotropic drugs.** Clinical Electroencephalography (Osaka). 17(4):199-207, 1975.

Electroencephalogram (EEG) changes induced by psychotropic drugs were studied in 21 mental patients with schizophrenia, manic-depression, psychogenic reaction and progressive paralysis who were treated with lithium, phenothiazine, butyrophenone, diazepam, and nitrazepam. Of the 21, 43% showed slow wave burst or spike and wave complex. Observations included minute changes in the basic wave, especially alpha waves, such as slowing of EEG, change in frequency of alpha wave, increase in frequency of alpha waves when closing or opening of eyes, flashing light stimulus or mathematical calculation. 11 references.

229907 Linnoila, M.; Saario, I.; Olkoniemi, J.; Liljequist, R.; Himberg, J. J.; Maki, M. Department of Pharmacology Siltavuorenpenger 10 A, Helsinki 17, SF-00170, Finland **Effect of two weeks' treatment with chlordiazepoxide or flupenthixole, alone or in combination with alcohol, on psychomotor skills related to driving.** Arzneimittel-Forschung (Aulendorf). 25(7):1088-1092, 1975.

The effects of 2 weeks' treatment with chlordiazepoxide (10mg oral dose daily) or flupenthixole (0.5mg oral dose daily) on human psychomotor performance related to driving was examined in 20 healthy male Ss aged 20 years to 23 years. The tests used were a choice reaction, two coordination tests and an attention test having correlation with traffic behavior. Neither chlordiazepoxide nor flupenthixole impaired psychomotor performance on the 7th or 14th days of the experiment. The combinations of either drug with 0.5g/kg of alcohol impaired coordination and attention to an extent considered dangerous for traffic and occupational life. Their interaction with alcohol was not so strong as that between diazepam and alcohol. The combination of chlordiazepoxide with alcohol also increased the anxiety of the normal Ss. 15 references. (Author abstract)

229924 Mendelson, Wallace B.; Reichman, John; Othmer, Ekkehard. Building 10, Room 3N 224, National Institutes of Health, Bethesda, MD 20014 **Serotonin inhibition and sleep.** Biological Psychiatry. 10(4):459-464, 1975.

In a study of serotonin inhibition and sleep, methysergide, a clinically used blocker of serotonin receptors, was given for 48 hr to 11 normal adults, at a dose of 8mg/24 hr. Total rapid eye movement sleep time was decreased, although total sleep time was unchanged. Stage 4 decreased and Stage 3 increased, while total slow wave sleep remained constant. There was a tendency toward a decrease in the number of intact sleep cycles. The relationship of these data to published reports on p-chlorophenylalanine is discussed. 14 references. (Author abstract modifed)

230781 Fink, Max; Irwin, Peter. Department of Psychiatry, State University of New York, Stony Brook, NY **Fenmetazole (DH-524): euphoriant classified by cerebral electrometry.** Current Therapeutic Research. 18(4):590-596, 1975.

The euphoriant effects of fenmetazole (DH-524) were classified by cerebral electrometry. The first phase in the electroencephalogram (EEG) profiling of fenmetazole (DH-524) was completed with 200mg determined as an active dose. Drug associated findings include increases in EEG amplitudes, 6 to 13 Hz activity, and in blood pressure; decreases in EEG frequency deviation, activity below 6 Hz and above 15 Hz, and in heartrate. Subject reports include head tingling and characterizations of fenmetazole as an up. Fenmetazole is assessed to be a euphoriant by EEG criteria, and clinical studies in neurotic depressed patients are recommended. 11 references. (Author abstract)

230830 Ghoneim, M. M.; Mewaldt, S. P.; Thatcher, J. W. Department of Anesthesiology, University of Iowa, Iowa City, IA 52242 **The effect of diazepam and fentanyl on mental, psychomotor and electroencephalographic functions and their rate of recovery.** Psychopharmacologia (Berlin). 44(1):61-66, 1975.

The effect of diazepam and fentanyl on mental, psychomotor and electroencephalographic (EEG) functions were examined. Ten healthy male subjects received diazepam, fentanyl or a placebo intravenously at weekly intervals according to a latin square design. They were tested on a battery of psychological and EEG tests at 0.5, 2, 6, and 8 hrs following injection. Fentanyl had little effect on memory while diazepam reduced the ability to learn without increasing forgetting of material already acquired. By the second hour post injection, only the low dose of fentanyl had no residual effect. Recovery was complete by the sixth hour for all treatments according to the psychological tests except for the lagging effect of high

dose of diazepam on memory. The EEG effects of diazepam persisted beyond the end of the testing sessions while those of the high dose of fentanyl recovered by the eighth hour. Thus in the dosages tested, diazepam had more intense and prolonged effects than fentanyl. 19 references. (Author abstract)

230863 Tecce, Joseph J.; Cole, Jonathan O.; Savignano-Bowman, June. Laboratory of Neuropsychology, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **Chlorpromazine effects on brain activity (contingent negative variation) and reaction time in normal women.** Psychopharmacologia (Berlin). 43(3):293-295, 1975.

Electrical brain activity (contingent negative variation or CNV) and psychomotor behavior (reaction time or RT) were measured after 50 mg of chlorpromazine (CPZ) or placebo were given orally to 28 normal women. CPZ reduced CNV 2 and 3 hrs postdrug and slowed RT 3 hrs postdrug. CNV amplitude appears to be an accurate indicator of drug produced changes in alertness. 10 references. (Author abstract)

230867 Risberg, Ann-Marie; Risberg, Jarl; Ingvar, David H. Laboratory of Clinical Neurophysiology, University Hospital, Lund, Sweden **Effects of promethazine on nocturnal sleep in normal man.** Psychopharmacologia (Berlin). 43(3):279-284, 1975.

The effects of a phenothiazine, promethazine, on sleep in 10 healthy volunteers were investigated in two double-blind polygraphic studies. The first part consisted of a single dose study with promethazine using pentobarbital as a reference substance. In the second part, four subjects spent 20 consecutive nights with nine drug nights (promethazine), followed by a placebo withdrawal period of six nights, in the sleep laboratory. Promethazine showed a dose related depressing effect with a greater decrease, the higher the dose. There was also an increase of stage 2 and with the highest dose an increase of stage 3 and 4. An increase of REM latency together with a decrease of REM periods was also seen, and while pentobarbital gave a decrease in REM density, promethazine did not cause any changes in the phasic REM component. The REM depressing effect of promethazine together with its relatively weak REM rebound effect may explain its value in the treatment of withdrawal symptoms following abuse of alcohol and barbiturates. 22 references. (Author abstract modified)

230871 Roth, Walton T.; Rosenbloom, Margaret J.; Darley, Charles F.; Tinklenberg, Jared R.; Kopell, Bert S. Department of Psychiatry, Stanford University Medical School, Stanford, CA 94305 **Marihuana effects on TAT form and content.** Psychopharmacologia (Berlin). 43(3):261-266, 1975.

In a study of marihuana effects on the Thematic Apperception Test (TAT) form and content, 72 normal male subjects were given either placebo or marihuana containing delta9-tetrahydrocannabinol. Stories written to cards selected from the Thematic Apperception Test did not differ on hostile or sexual content scales between drug and placebo conditions, but 6 out of 10 scales specifically constructed to detect marihuana effects were successful at differentiating the two conditions. Under marihuana, the stories had a timeless, nonnarrative quality, with greater discontinuity in thought sequence and more frequent inclusion of contradictory ideas. Novelty of content was somewhat increased by marihuana, while relation of the picture, imagery, repetition, and closure were not significantly affected. 19 references. (Author abstract)

231066 Hammond, Kenneth R.; Joyce, C. R. B. University of Colorado, Boulder, CO 80302 **Psychoactive drugs and social judgment: theory and research.** Wiley Series on Personality Processes. Somerset, NJ, Wiley-Interscience, 1975. 288 p. $16.95.

New theory and research methods on the effects of psychoactive drugs on sociophysiological behavior are reported. The studies support the thesis that psychoactive drugs have a deleterious effect on human judgment, interpersonal conflicts, and interpersonal learning of both hospitalized and normal patients.

231629 Porges, Stephen W.; Walter, Gary F.; Korb, Robert J.; Sprague, Robert L. Deparmtnet of Psychology, University of Illinois, Champaign, IL 61820 **The influences of methylphenidate on heart rate and behavioral measures of attention in hyperactive children.** Child Development. 46(3):727-733, 1975.

Reaction time performance and heartrate responses associated with attention were used to assess the hyperactive child's attentional deficit and his response to methylphenidate. Attentional deficits shown by long response latencies were reflected in heartrate responses theoretically incompatible with sustained attention. Ss exhibiting the greatest attentional deficit displayed the most favorable response to methylphenidate in both reaction time performance and physiological measures. Ss who showed the greatest improvement in social behavior were those who showed the least improvement in reaction time performance. 26 references. (Author abstract)

232364 Kruskemper, Gertrud; Kruskemper, Hans L. II. Medizinische Universitatsklinik, Dusseldorf, Moorenstr. 5, Germany **/Psychological analyses of patients suffering from hypothyroidism./** Psychologische Verlaufsuntersuchungen bei Unterfunktion der Schilddruse. Zeitschrift fur psychosomatische Medizin und Psychoanalyse (Gottingen). 20(1):37-52, 1974.

Three personality inventories and a complete psychological history were obtained on seven adult patients suffering from late acquired, primary hypothyroidism before medical treatment and after 12 to 20 months of thyroxine therapy. Specific patterns of performance and emotional status were determined in these patients. The intellectual quotients (IQ) were not normally distributed, and there were no above average IQs before therapy. Intelligence subscales with time limitations showed results in very low intelligence classes, thereby confirming the anamnestic findings that patients were unable to adequately perform in their daily life scores. The tendencies toward neurotic reactions were elevated before treatment. Retardation of mental and motoric processes and the characteristically uncomplaining attitude of the patients lead to misinterpretation of the severity of their emotional problems in a normal medical examination. Under thyroxine therapy, these alterations are reversible to a large extent. 22 references. (Journal abstract modidied)

232518 Carpenter, John A.; Gibbins, Robert J.; Marshman, Joan A. Center of Alcohol Studies, Rutgers Univ., New Brunswick, NY 08903 **Drug interactions: the effects of alcohol and meprobamate applied singly and jointly in human subjects. II. Five experiments.** Journal of Studies on Alcohol. Supplement No. 7:54-139, 1975.

Five experiments were conducted to study the effects of alcohol and meprobamate, administered snngly and in combina-

tion, at doses up to 1.20g of alcohol per kg of bodyweight and up to 30mg of meprobamate per kg. Most of the male Ss were of college age (range, 21-49). In all experiments behavior was tested with a simple motor coordination task. All analyses were carried out on the postdrinking behavior, corrected for predrinking performance. Blood samples were obtained in all experiments. Results are presented as conventional analyses of variance. Blood levels of the two drugs are listed, followed by the behavioral measures. In experiments 4 and 5 some of the results are presented as three dimensional isometric figures. All behavioral measures were analyzed as a function of the drug doses and are presented in that form. The overall conclusion is that the prolonged administration of meprobamate had an ameliorating effect on alcohol produced changes in behavior and that a single dose increased the absorption of alcohol. 35 references.

232519 Ashford, J. R.; Cobby, J. M. Dept. of Mathematical Statistics and Operational Research, Univ. of Exeter, Exeter,, Devon, England **Drug interactions: the effects of alcohol and meprobamate applied singly and jointly in human Subjects. III. the concentrations of alcohol and meprobamate in the blood and their effects on performance; application of mathematical models.** Journal of Studies on Alcohol. Supplement No. 7:140-161, 1975.

The relations between the levels of alcohol and meprobamate in the blood and performance on a visual/motor coordination tracking task were analyzed by a general system of mathematical models, using data from Experiment V by Carpenter et al. (pp. 54-139). The derivation of the models is described in general; the relationship between blood alcohol concentration; (BAC) and performance was nonmonotonic: best performance occurred at BACS of 10mg to 20mg per 100ml. The relationship between meprobamate concentration (BMC) and performance was monotonic: performance deteriorated with increasing BMC. The results of the reaction latency measure, however, showed no consistent relationship with BAC or BMC. The action of alcohol can be represented by a model which involves two distinct sites of action; that of meprobamate one site. The implications of the results are discussed, with particular reference to the quantitative description of the joint action of drugs and the design of future experiments. 8 references. (Author abstract modified)

232521 Ashford, John R.; Carpenter, John A. Dept. of Mathematical Statistics and Operational Research, Univ. of Exeter, Devon, England **Drug interactions: the effect of alcohol and meprobamate applied singly and jointly in human subjects. V. Summary and conclusions.** Journal of Studies on Alcohol. Supplement No. 7:177-187, 1975.

The design, analysis and conclusions of the series of experiments by Carpenter et al.,Ashford and Cobby, and Cobby and Ashford are reviewed. Mathematical models of the joint action of drugs were developed and data obtained to test the models by studying the action of alcohol and meprobamate singly and in combination in human subjects. The data proved to be too limited in the range of drug concentrations in the blood necessary to identify the single most appropriate model. The majority of the results of the two analyses agreed; however, in experiment 5 Carpenter et al. combined drugs, doses and blood samples in one analysis and found a significant influence of meprobamate dose on blood alcohol concentration and homogeneous error terms. Theoretically the models can analyze the pattern of behavioral results at each combination of doses but the data available were insufficient for the purpose. The modifications in experimental design and analytical techniques necessary to continue research in developing mathematical models are discussed. (Author abstract modified)

232532 Saletu, B.; Saletu, M.; Herrmann, W. M.; Itil, T. M. Psychiatrische Universitatsklinik, Abt. fur Pharmakopsychiatrie, Lazarettgasse 14, A-1097 Vienna, Austria **Are hormones psychoactive? Evoked potential investigations in man.** Arzneimittel-Forschung (Aulendorf). 25(8):1321-1327, 1975.

At the 16th Annual Alpine EEG Meeting, held in Zurs, Austria, in the winter of 1974, a study was reported in which the somatosensory evoked potential (SEP) of physically and mentally healthy male subjects was recorded before as well as 4 hours after administration of one single dose of placebo, cyproterone acetate (an antiandrogen), and mesterolone (an androgen). Quantitative evaluation of drug induced changes in SEP latencies and amplitudes, did not demonstrate any significant alterations after placebo. Contrary to this, cyproterone acetate induced systematic and significant changes in SEP profiles. Mesterolone, on the other hand, produced a significant latency decrease in the late part of the evoked response. Based on stepwise discriminant analysis of these data both hormones were significantly differentiated from placebo as well as from each other. It is concluded that cyproterone acetate reveals anxiolytic qualities and mesterolone exhibits antidepressant ones. 91 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

225686 Lapierre, Y. D. Dept. of Psychiatry, University of Ottawa, Ottawa, Ontario, Canada **/Evaluation of side-effects on neurotics -- a test using mesoridazine and placebo./** Evaluation des effets secondaires chez les nevrotiques -- un essai avec la mesoridazine et le placebo. Canadian Psychiatric Association Journal (Ottawa). 20(1):61-66, 1975.

The incidence of side-effects following administration of mesoridazine and placebo was studied in a neurotic outpatient population using an open questionnaire and a symptom checklist. Men on mesoidazine reported more side-effects with a symptom checklist than on the questionnaire. The difference was not considered significant in women. More symptoms were elicited with a checklist while the patients were on the drug than by questioning. The side-effects were mainly gastrointestinal and mild. Cardiovascular symptoms were as frequent on placebo as on the active drug. After 6 weeks of double-blind administration no difference was found in the total number of side-effects reported for placebo and for mesoridazine. (Author abstract)

225699 Misra, P. C. Hollymoor Hospital, Birmingham, B31 5EX, England **Nitrazepam (Mogadon) dependence.** British Journal of Psychiatry (London). 126:81-82, 1975.

The addictive characteristics of a psychological dependence on nitrazepam (Mogadon) are examined and documented in a case study of a female patient. The patient developed an intense dependence on nitrazepam after its use in treating her insomnia, so that she could not live a normal life without this drug. Symptoms of depression, anxiety, and agitation occurred immediately after the drug was discontinued, and on two occasions these symptoms were relieved by its reinstatement. It is proposed that these were withdrawal symptoms. It is suggested that when prescribing nitrazepam, the vulnerable personality of the patient should be kept in mind. 8 references. (Author abstract modified)

225722 Swett, Chester, Jr. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Rd., Waltham, MA 02154 **Drowsiness due to chlorpromazine in relation to cigarette smoking: a report from the Boston collaborative drug surveillance program.** Archives of General Psychiatry. 31(2):211-213, 1974.

The frequency of drowsiness attributed to orally administered chlorpromazine hydrochloride was compared among 130 nonsmokers, and 201 light, and 72 heavy cigarette smokers. It was found that drowsiness occurs in 16%, 11%, and 3% respectively. The findings suggest that the clinical effects of chlorpromazine may be influenced by cigarette smoking. Reasons suggested for the results reported are that the personalities of smokers are different from nonsmokers, that the propensity for drowsiness is greater in nonsmokers, it is surmised that more rapid metabolism of chlorpromazine in cigarette smokers may be a factor. 9 references. (Author abstract modified)

225873 Blazer, Dan G.; Haller, Lee. Dept. of Psychiatry, Duke University Medical Center, Box 3812, Durham, NC 27710 **Pentazocine psychosis: a case of persistent delusions.** Diseases of the Nervous System. 36(7):404-405, 1975.

A case of psychosis secondary to pentazocine is presented. The patient demonstrated hallucinations, perceptual aberrations, a distorted body image and delusional thinking. The delusional ideation persisted for a period of three weeks. It is noted that such a case of persistent delusional thinking secondary to pentazocine administration has not been reported previously. Mechanisms of action are postulated, and physician awareness of these side-effects is recommended. 11 references. (Author abstract modified)

225890 Ahmad, S.; Laidlaw, John; Houghton, G. W.; Richens, A. National Hospitals-Chalfont Centre for Epilepsy, London, England **Involuntary movements caused by phenytoin intoxication in epileptic patients.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(3):225-231, 1975.

The case histories of four patients who developed choreoathetoid movements during intoxication with phenytoin are presented. Drug intoxication was confirmed in each case by measuring the serum phenytoin concentration. Drug interactions were, in part, responsible for the occurrence of intoxication in three patients. It is pointed out that phenytoin intoxication is not always easy to recognize, particularly when nystagmus is minimal or absent, as in these four patients. The estimation of the serum phenytoin concentration is recommended in this situation. 26 references. (Journal abstract modified)

226828 Gasser, J. Conrad; Kaufman, Robert D.; Bellville, J. Weldon. Department of Anesthesiology, Kantonsspital, Zurich, Switzerland **Respiratory effects of lorazepam, pentobarbital, and pentazocine.** Clinical Pharmacology and Therapeutics. 18(2):170-174, 1975.

The respiratory effects on six male volunteers of a new benzodiazepine, lorazepam, were compared to those of pentobarbital and pentazocine. Pentobarbital, 50 and 150mg, produced respiratory depression, as did pentazocine, 30mg intramuscularly. Lorazepam at 1.33 and 4mg intramuscularly produced none. 10 references. (Author abstract)

226897 Rack, P. H.; Vaddadi, K. Lynfield Mount Hospital, Heights Lane, Bradford 8, England **Side effects of tricyclic antidepressant drugs with particular reference to dothiepin.** International Pharmacopsychiatry (Basel). 10(3):129-136, 1975.

Fifteen patients on dothiepin and 20 on other tricyclic compounds were compared for side-effects by self-rating. The high incidence of complaints beforehand and overall reduction during 2 weeks of treatment, correlating with clinical improvement, shows that comparison of side-effects is unreliable unless pretreatment incidence is recorded. 9 references. (Author abstract)

226922 Judd, Lewis L.; Grant, Igor. Department of Psychiatry, University of California, San Diego, School of Medicine, La Jolla, CA 92037 **Brain dysfunction in chronic sedative users.** Journal of Psychedelic Drugs. 7(2):142-149, 1975.

Brain dysfunction was examined in chronic sedative users. Half of the polydrug users demonstrated cerebral dysfunction. When the adaptive abilities of polydrug users were compared to those of medical and neurological patients, there was a continuum from no impairment in the medical group through moderate impairment in polydrug users to severe impairment among neurological patients. The central nervous system depressant users showed the most marked neuropsychological deficits in the following areas of cognitive functions: 1) concept formation and ability to abstract; 2) nonverbal learning; 3) perceptuomotor coordination; 4) accuracy of perception; and 5) speed of motor movement. 15 references.

227136 Penttila, Antti; Lehti, Heikki; Lonnqvist, Jouko. Department of Forensic Medicine, University of Helsinki, Kytosuontie 11, SF-00280 Helsinkie 28, Finland **Psychotropic drugs and impariment of psychomotor functions.** Psychopharmacologia (Berlin). 43(1):75-80, 1975.

The effects of psychotropic drug therapy on the operation of psychomotor functions used in a clinical examination of suspected drunken drivers were studied. One hundred psychiatric mental, but otherwise healthy, patients were examined; the type of medication and the number of drugs used varied greatly. In 71 cases the mean degree of error in the clinical examination was higher, and, in several of these, markedly higher than the reference values obtained eariler on suspected drunken drives when the blood contained very small amounts of alcohol or none at all. In 18 cases coarsely divided nystagmus was registered in patients on psychotropes. This is an obvious sign of a marked side-effect of medication but was present more infrequently than in subjects with after ingestion of alcohol. The present results indicate that application of the clinical examination method, which was originally developed for an related to the examination of alcohol cases, to subjects on psychotropes is adequate, and it is possible with clinical examination to obtain valuable medicolegal information on the impairment of physiological functions. 27 references. (Author abstract modified)

227745 Thornton, William E.; Pray, Bonnie J. Illinois Drug Abuse Programs, Chicago, IL **Lithium intoxication: a report of two cases.** Canadian Psychiatric Association Journal (Ottawa). 20(4):281-282, 1975.

Two cases of severe lithium intoxication are reported. The first patient displayed symptoms resembling those of organic brain syndrome which was not associated with a high serum lithium level. The influence of diuretic therapy in combination with lithium is thought to enhance the risk of intoxication. The second case depicts acute central nervous system toxicity with known fatal potential. Conservative lithium administration is recommended for acute psychosis and the beneficial effects of urea and aminophylline on renal lithium elimination in the active treatment of lithium poisoning are noted. 13 references. (Author abstract modified)

227808 Ogura, Chikara; Kuda, Kenji; Akamatsu, Tetsuo; Okuma, Teruo; Setogawa, Tomoichi; Tamai, Akihiko; Matsuura, Hiroyuki; Kuba, Shusaku. Department of Neuropsychiatry, School of Medicine, Tottori University, Japan **Ophthalmological findings on neuropsychiatric patients during psychopharmacotherpy: II. Seven cases due to antipsychotic drugs.** Clinical Psychiatry (Tokyo). 17(3):271-281, 1975.

Lenticular opacities, seemingly induced by psychopharmacological treatment in mental patients, are discussed. Among 313 mental patients who had been treated with psychotropic drugs, three males and four females were found to have ocular opacities. Of these patients, six were schizophrenics, and one was a manic-depressive. The patients ranged in age from 12 to 49 years (average age of 32.9years), and had illnesses of 1 to 26 years' duration (average duration 11.9years). The seven patients had milky white on greyish white dots, dust or starfish shaped opacities at the surface of the pupils. Lenticular and corneal opacities were more frequently observed among patients with dark skin pigmentation. A higher frequency of this side-effect was observed among patients treated with charge, long-term doses of chlorpromazine, levomepromazine and perphenazine than among others. 25 references.

228072 Suh, Kwang Youn. Department of Neuro-psychiatry, College of Medicine, Han Yang University, Korea **Two cases of convulsions during lithium therapy.** Korean Central Journal of Medicine (Seoul). 28(3):289-292, 1975.

Two cases of convulsions with semicomatose conditions during lithium carbonate treatment are reported. In the first case, a man, aged 32, developed typical grand mal like seizures after 8 days of treatment with 1200mg lithium and 300mg of chlorpromazine daily. In the second case, a man, aged 34, developed the same manifestations except for the occurrence of a seizure attack after 17 days of treatment. The convulsive attacks and semicomatose conditions disappeared immediately after withdrawal of lithium. The development of convulsions in both cases were concluded not to be related to the overdosage of lithium. 17 references. (Journal abstract)

228208 Johnstone, Eve C.; Whaley, K. Div. of Psychiatry, Clinical Research Centre, Horrow, Middlesex, England **Antinuclear antibodies in psychiatric illness: their relationship to diagnosis and drug treatment.** British Medical Journal (London). No. 5973:724-725, 1975.

The incidence of serological evidence of systemic lupus erthematosus in 100 patients with acute psychiatric conditions was compared with its incidence in controls. The relationship between the presence of antinuclear factor and (a) the psychiatric diagnosis and (b) the drug history are examined. Antinuclear antibodies occurred more often and in higher titers in psychiatric patients than in controls. Anti-deoxyribonucleic acid antibodies were not found. It is suggested that antinuclear antibodies may be drug induced and that lithium carbonate may have a particular tendency to produce this reaction. 14 references. (Author abstract modified)

228214 Miura, Sadanori; Suzuki, Tooru; Sakurai, Shunsuke. Department of Neuro-psychiatry, Kitazato University School of Medicine, Kanagawa, Japan **Review of long-term psychiatric medication - a study of withdrawal symptoms.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1313-1325, 1974.

The literature on relapse of mental illness after cessation of psychopharmaceutic therapy is reviewed. Frequency of occurrence of relapse of mental illness during irregular administration of drugs, after termination of medication and during continuous medication is considered. Withdrawal symptoms of various psychotropic drugs and antiparkinsonism agents are also discussed. 62 references.

229039 Cushman, P.; Grieco, M.; Gupta, S. St. Luke's Hospital Center, New York, NY 10025 **Reduction in T-lymphocytes forming active rosettes in chronic marijuana smokers.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):217-220, 1975.

Rosettes formed by peripheral thymus dependent (T) and thymus independent (B) lymphocytes were studied in 23 normal controls and 23 marihuana smokers. The mean percentage of cells B-type rosettes were normal in both groups. The percentage of T-cells forming rosettes was lower in the marihuana smokers, and 39% had values below two standard deviations of the mean of the normal control group. These observations suggest some alteration in some T-cells in some marihuana smokers. 9 references. (Author abstract)

229118 Arseni, C.; Dragulea, G.; Alexianu, D. Clinica de neurochirurgie, Bucharest, Rumania **/Relationships between anesthetic substances, convulsions, and psychic disturbances./** Relatii intre substantele anestezice, convulsii si tulburari psihice. Neurologie, Psihiatrie, Neurochirurgie (Bucuresti). 20(2):129-134, 1975.

Relationships between anesthetic substances, convulsions and mental disorders were discussed. A large number of psychotropic and anesthetic drugs, acting at different levels of the central nervous system either by depression or cataleptic excitation can either facilitate or determine the occurrence of clinical epileptiform attacks, confirmed by electrocardiogram or manifested only in the electroencephalogram (EEG) even in patients with convulsive antecedents. Some morphinomimetic analgesics exert their action through the alteration of the convulsive threshold at the level of the limbic system, and these effects are used in the drug activation for the localization of EEG of epileptic foci. In epileptic patients, general anesthesia involves the risk of intraanesthetic and postanesthetic accidents, and the possibility of more severe mental manifestations improved by cerebral dehydration and administration of diazepam. 19 references. (Journal abtract modified)

229169 Wildman, Robert W.; Wildman, Robert W., II. Central State Hospital, GA **An investigation into the possibility of irreversible central nervous system damage as a result of long-term chlorpromazine medication.** Journal of Clinical Psychology. 31(2):340-344, 1975.

An experiment was conducted to determine whether the behavioral deficits manifested by patients on chlorpromazine were temporary or permanent. Four groups of inpatients at a state hospital, including schizophrenics and patients with organic central nervous system damage, were administered a series of tests selected for their ability to differentiate between organic and psychiatric patients. Results indicate that of the five tests used, two tests significantly differentiated the organics from the schizophrenic controls -- the Spiral Aftereffect and the Porteus Maze tests. Findings show that the schizophrenic group no longer on chlorpromazine showed no significant impairment on any of the tests when compared with the schizophrneic control group that had received little or no chlorpromazine. It is concluded that: (1) no permanent impairment due to chlorpromazine was demonstrated; and (2) since patients who were receiving chlorpromazine were impaired, the drug may cause distortions on psychological tests and may create difficulty in responding properly to psychotherapy. The

question whether high dosage over a long period of time causes irreversible impairment remains yet to be determined. 10 references. (Author abstract modified)

229350 Saxen, Irma; Saxen, Lauri. Third Department of Pathology, University of Helsinki, SF-00290 Helsinki 29, Finland **Association between maternal intake of diazepam and oral clefts.** Lancet (London). 2(7933):498, 1975.

Data were collected on mothers of 599 children with oral clefts and on 590 matched controls to investigate a suspected association between maternal intake of benzodiazepines during the first trimester of pregnancy and oral clefts in the children. Between the group of clefts with additional defects and their controls no difference in the intake of benzodiazepines could be seen. Maternal memory bias and chance correlations were ruled out as factors. Confounding factors such as maternal illness and consumption of other drugs have not yet been ruled out and call for further investigation. 3 references.

229369 Arguelles, A. E.; Rosner, J. Clinical Pharmacology and Stress Unit, Hospital Aeronautico, D.I.G.I.D. (Ministry of Defence), Buenos Aires, Argentina **Diazepam and plasma-testosterone levels.** Lancet (London). 2(7935):607, 1975.

Plasma testosterone levels were measured in a sample of 35-55-year-old men, with minor complaints of nervousness or mental tension, to determine the effect of diazepam on sexual behavior. When these subjects were taking 10-20mg/day of diazepam orally for 2 weeks, plasma testosterone levels were significantly increased. A small but not significant reduction in plasma-11-hydroxycorticoid concentration was observed. Findings suggest more general endocrine changes associated with the intake of diazepam. 1 reference.

229549 Paroli, Eugenio. Universita degli Studi di Roma, Istituto di Farmacologia Medica II, Rome **/Pharmacological and toxicological problems connected with the use of long-acting neuroleptics./** no title Rivista di Psichiatria (Roma). 10(1):21-26, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October, 1974, pharmacological and toxicological problems connected with the use of long-acting neuroleptics were discussed. The neuroleptics may induce extrapyramidal side-effects to a degree in which their antidopaminergic properties dominate anticholinergic activity. Drugs discussed include chlorpromazine, fluphenazine decanoate, apomorphine, phenothiazines, thioridazine, clozapine, haloperidol, and spiroperidol. The tendency toward parkinsonism with neuroleptics could be correlated both with the individual metabolism of DOPA and with the efficiency of acetylcholine synthesis in the extrapyramidal nervous system. 15 references.

230012 Ananth, J. St. Mary's Hospital, 3830 Lacombe Avenue, Montreal, Quebec **Congenital malformations with psychopharmacologic agents.** Comprehensive Psychiatry. 16(5):437-445, 1975.

Studies reporting fetal effects, particularly teratogenesis, of psychopharmacological agents are examined in a literature review. Antidepressants, lithium, hypnotics, anxiolytics, alcohol and lysergic acid diethylamide (LSD) are among the drugs examined. An extensive review of congenital malformations in the infants of women who received psychopharmacologic agents during pregnancy reveals the occurrence of very few cases of congenital defects. Present evidence does not preclude prescription of psychopharmacologic agents to pregnant women with mental illness or epilepsy. Reduction of drug induced malformations is discussed in terms of careful prescribing and monitoring of drug effects as well as central recording by a registry. 62 references.

230027 Larned, Deborah. no address **Do you take Valium?** Ms. 4(5):26-30, 1975.

Dangerous side-effects from the therapeutic use of Valium, a benzodiazepine compound, are discussed, stressing that its versatility and capacity to relieve a variety of physical and psychological symptoms have made it the most widely prescribed drug of any kind in the world. Its capacity to relieve anxiety and other tension related disorders without serious interference with alertness has led physicians to overprescribe it in many cases. As a powerful central nervous system depressant, its side-effects include fatigue, drowsiness and ataxia even in relatively small doses. It also has many paradoxical effects, such as producing insomnia if taken as a sleeping pill in large doses over an extended period of time. Hostility and rage are also found in some cases, and overdose can easily result in death. It is noted that because of recent reports of tranquilizer abuse and due to its dependency liability, new Federal restrictions were placed on prescriptions under the Controlled Substances Act of 1970. However, even further caution is needed, particularly a warning label similar to the one that now accompanies birth control pills and other potentially harmful drugs.

230424 Cole, A. P.; Hailey, D. M. Dept. of Paediatrics, St. George's Hospital, London, England **Diazepam and active metabolite in breast milk and their transfer to the neonate.** Archives of Disease in Childhood (London). 50(9):741-742, 1975.

Nine breast feeding mothers were given diazepam for postpartum tranquillization of persistent hypertension, and levels of diazepam and its metabolite, desmethyldiazepam, were assayed in samples of the mother's milk, blood, and the blood of the infant. No adverse clinical effects were observed other than three cases of jaundice. Varying levels of diazepam were found in the mothers' milk and blood. Measurable blood levels of the compounds were found in the breast fed neonates. the infants metabolized these drugs more slowly than adults, making accumulation in the infant possible. 6 references. (Author abstract modified)

230580 Elithorn, Alick; Lunzer, Michael; Weinman, John. Department of Psychological Medicine, Royal Free Hospital, Pond Street, London, N.W. 3 **Cognitive deficits associated with chronic hepatic encephalopathy and their response to levodopa.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(8):794-798, 1975.

Computerized techniques were used to describe the cognitive deficits associated with chronic hepatic encephalopathy, and to assess the effects of levodopa therapy on this condition. A battery of computer based psychological tests given to seven patients with chronic hepatic encephalopathy showed them to be intellectually impaired, particularly on speed based measures, as compared with general hospital patients and with patients with cirrhosis but without clinical or encephalographic evidence of encephalopathy. The effects of levodopa were also evaluated by sequential assessment with these tests. Although there was some improvement in speed of performance on certain tasks and a suggestion of deterioration on other measures, there was little overall change. It is concluded that levodopa has an arousing or antidepressant action and that its effect on intellectual functions is secondary to this

alerting effect and is consequently dependent on the emotional status of the patient. 21 references. (Author abstract modified)

230742 Kellett, J. M.; Metcalfe, M.; Bailey, J.; Coppen, A. J. Department of Psychiatry, St. George's Hospital, London **Beta blockade in lithium tremor.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 38(7):719-721, 1975.

Practolol, propranolol, and placebo were tested on an objective test of lithium induced tremor. Both beta-blocking agents produced significantly more tremor than the placebo. It is argued that lithium induced tremor is closer to essential than to physiological tremor. 19 references. (Author abstract)

230820 Bickel, M. H. Medizinisch-chemisches Institut, University of Bern, Bern, Switzerland **Poisoning by tricyclic antidepressant drugs: general and pharmacokinetic considerations.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(2):145-176, 1975.

The general and pharmacokinetic considerations of poisoning by tricyclic antidepressants are presented. Tricyclic antidepressant drugs are frequently involved in intentional overdosage by depressed patients and in accidental poisoning by small children. Toxicological and pharmacokinetic aspects of thymoleptics are discussed with respect to the severely intoxicated patient and his treatment. 223 references. (Author abstract modified)

231317 Biamino, G.; Fenner, H.; Schuren, K. -P.; Neye, J.; Ramdohr, B.; Lohmann, F. -W. Department of Cardiology, Klinikym Steglitz, Berlin, Germany **Cardiovascular side effects of tricyclic antidepressants -- a risk in the use of these drugs.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 11(3):253-261, 1975.

The influences on myocardial contractility of cat papillary muscle induced by imipramine and dimetacrine as well as their desmethyl compounds. The effects of i.v. administration of imipramine and dimetacrine on cardiovascular functions were investigated in 18 patients at cardiac catheterization. In addition four patients were studied during ergometric exercise before and 45 min after injection of both drugs. Finally, fluorimetric determination of norepinephrine plasma concentrations were carried out in eight patients. Results indicate that imipramine and dimetacrine have a striking dose dependent negative inotropic effect on cat papillary muscle; the effect of the desmethyl compounds was less significant. In man, imipramine and dimetacine did not significantly influence heartrate or cardiac index but did induce an increase in mean systemic pressure which was accompanied by a marked increase in norepinephrine plasma levels. It is concluded that these tricyclic antidepressants have an unequivocal negative inotropic effect and that, in view of these cardiovascular side-effects, their use is contraindicated in patients predisposed to myocardial failure. 36 references. (Author abstract modified)

231991 Kline, Nathan S.; Angst, Jules. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY 10027 **Side effects of psychotropic drugs.** Psychiatric Annals. 5(11):8-12, 15-16, 21-22, 24, 17-29, 33-35, 38-39, 1975.

Some of the adverse reactions to and side-effects of the most frequently prescribed psychotropic drugs are reviewed by examining the literature. Side-effects of tricyclic antidepressants, lithium, monamine oxidase (MAO) inhibitors, antiparkinson drugs and the phenothiazines are summarized. It is noted that urinary retention, blood pressure, body temperature, and cardiovascular effects are often noted at the beginning of psychopharmacologic treatment. Visual and autonomic effects of psychotropic drugs are discussed, along with irregularity, nausea, and loss of weight, which are among the gastrointestinal symptoms not frequently reported. Changes in hepatic function and neurological, endocrinological, dermatological, and hematologic effects are described in detail. The slight possibility of sudden death or miscarriage related to drug treatment is also explored. Acute psychological reactions such as oversedation, depression, mood change, manic syndromes and delirious states are also briefly considered. 114 references.

231992 Kellner, Robert. Department of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM 87106 **Unwanted effects of minor tranquilizers and hypnotics.** Psychiatric Annals. 5(11):43-44, 47-49, 1975.

Side-effects of a few of the more commonly used minor tranquilizers, including Librium (chlordiazepoxide) and Valium, (diazepam) are described. Uncomfortable reactions including ataxia, anxiety, drowsiness and allergic reactions are examined for each drug. The central nervous system side-effects of meprobamate are also listed. It is noted that benzodiazepines can lead to depression, hostility, habituation or even addiction. Several frequently reported cross-tolerances and dangerous drug interactions and combinations are considered. It is noted that tolerance develops after prolonged use of drugs such as chloral hydrate, barbiturates and the nonbarbiturate hypnotics. A few helpful suggestions are made to patterns for the prevention of drug dependence. 53 references.

231993 Simpson, George M. Dept. of Psychiatry, New York Medical College, New York, NY **CNS effects of neuroleptic agents.** Psychiatric Annals. 5(11):53-54, 59-60, 1975.

The unwanted neurological and central nervous system (CNS) effects of neuroleptic or antipsychotic agents are described. Five groups of neuroleptics which produce extrapyramidal disorders are discussed, and it is concluded that neuroleptics generally provide safe and effective treatment, although side-effects do occur. It is noted that some abnormal behavioral effects can take place in a small percentage of subjects with almost any drug. Extrapyramidal effects are frequent, but with the exception of tardive dyskinesia, are usually easy to manage. It is conceded that grand mal and temporal lobe disturbances can occur and withdrawal effects (particularly if an antiparkinsonian agent is also being given) can take place. Several suggestions for treatment of severe or gross over-dosages are provided. 16 references. (Author abstract modified)

231994 Sugerman, A. Arthur. Carrier Clinic, Belle Mead, NJ **Non-CNS side effects of neuroleptics.** Psychiatric Annals. 5(11):61, 64-65, 69-70, 1975.

A few of the various noncentral nervous system reactions to neuroleptics in some patients are examined. Side-effects are described under the following headings: exaggerations of normal pharmocodynamic effects, allergic reactions, and effects following long-term use of phenothiazines. It is concluded that most of the side-effects of antipsychotic drugs manifested outside the central nervous system are annoying but not serious; some simple measures can prevent life threatening complications. It is felt that an awareness of the side-effects that can be produced by the different classes of antipsychotics is important. Recommended dosage and combinations of drugs to be avoided are discussed in some detail. The trade names of some common neuroleptics are also listed in tabular form. 4 references. (Author abstract modified)

231995 Mielke, David H. Tulane University School of Medicine, New Orleans, LA 70118 **Adverse reactions associated with mood-altering drugs.** Psychiatric Annals. 5(11):71-73, 77-79, 83-86, 89, 1975.

Adverse reactions, poisoning, and the clinical management of antidepressants and lithium threatment in both adults and children are discussed. Three tables summarizing the side-effects of tricyclic antidepressants, the monoamine oxidase (MAO) inhibitors, thymoleptic drugs and lithium are included. It is concluded that thymoleptic drugs are generally safe and efficacious in inducing symptomatic relief when administered to appropriate patients. It is anticipated that adverse reactions and poisoning will continue to be a problem, as greater amounts of these drugs are being dispensed each year. It is felt that proper patient supervision reduces the risks associated with the use of these potent compounds; thus a preventive approach, together with thoughtful patient selection, is recommended. Treatment of toxic reactions from various drug combinations and interactions are also considered. 47 references. (Author abstract modified)

232260 Diehl, L. W. Psychiatrische Klinik der Freien Universitat, 1 Berlin 19, Nussbaumallee 36 **/The therapy of autonomic regulatory disturbances through drugs./** Therapie vegetativer Fehlsteuerung durch Medikamente. Therapie der Gegenwart (Munchen). 113(10):1668, 1670-1672, 1675-1677, 1680, 1682, 1685-1686, 1688, 1974.

The widespread use of psychopharmaceuticals, especially in the treatment of autonomic regulatory disturbances, is discussed. The effects of commonly used drugs are evaluated, with special emphasis on possible adverse reactions, dependency, or addiction. It is suggested that in cases where a psychotherapeutic approach is indicated, drugs which suppress the symptoms of underlying disturbances should not be administered as they will tend to complicate effective diagnosis and treatment. It is concluded that use of drugs, especially the tranquilizers and antidepressants, should not be considered a long-term therapeutic technique, as they are never without undesirable side-effects. 50 references.

16 METHODS DEVELOPMENT

226725 Itil, T. M. no address **Psychotropic drugs and the human EEG.** Modern Problems of Pharmacopsychiatry. Basel, S. Karger, 1974. 377 p. Vol. 8. $54.75

The relationship between psychotropic drugs and the human electroencephalogram (EEG) is reviewed. Qualitative EEG findings with the major tranquilizers, circulatory drugs, and caffeine, nicotine and alcohol are presented. A variety of techniques such as digital period analysis, power spectrum analysis and amplitude integration are described. It is suggested that these techniques provide a systematic method of classifying psychoactive drugs. A classification of psychotropic drugs based on computer classified sleep stages is also attempted. Based on observations of typical evoked potential changes induced by representatives of different psychopharmaceutical classes, a method to predict psychoactive properties of newly developed compounds is presented. Three papers on EEG correlates of behavior which indicate that the EEG might eventually become a valuable tool available to the psychiatrist are provided.

226902 Hanlon, Thomas E.; Blatchley, Robert J.; Kurland, Albert A. Maryland Psychiatric Research Center, Baltimore, MD 21228 **Effects of control techniques on therapeutic outcome in a controlled clinical trial.** International Pharmacopsychiatry (Basel). 10(3):169-176, 1975.

The effectiveness of a doctor's choice (DC) method of administering psychotropic drugs was compared to an experimentally determined treatment regimen employing random assignment and double-blind procedures. The 32 day drug trial sought to determine the comparative effectivness of thioridazine - placebo, thioridazine - chlordiazepoxide, and thioridazine - imipramine, with the daily dosage of openly administered thioridazine ranging from 100-900mg and dosages for chlordiazepoxide and imipramine, administered in a double-blind fashion, fixed at daily dosages of 30 and 75mg, respectively. DC medication, consisting of a choice (by a research physician) of any of the three experimental medications determined on the basis of judged clinical need, was added as a fourth treatment category for present purposes. Criteria of effectiveness included standardized psychiatric rating scales and global measures of improvement completed by research team members and ward physicians. Outcome results for the DC group compared to those for a single control group made up of individuals matched with DC patients on the basis of drug assignment indicate an essentially similar clinical effectiveness under both DC and control treatment conditions. 6 references. (Author abstract modified)

227213 Hamilton, M. University of Leeds, England **The methodology of trials of anti-depressants for depressed in-patients.** Journal of International Medical Research (Northampton). 3(Suppl. 3):64-69, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the problems involved in designing and recording trials in depressive drugs were discussed. An initial difficulty is one of classification and selection of suitable patients for admission to the trial. Contributing factors influencing the outcome are the time of hospitalization, previous exposure to similar therapy and the nature of the treatment given to the control group. An essential factor in trials of these drugs is the exclusion of the at risk suicide patient. Assessment has been made by more sophisticated rating scales, and the proper use of statistical analysis makes the results more valid than previously. (Author abstract modified)

227223 Frank, P. I. Manchester, England **Testing psychotropic drugs in general practice.** Journal of International Medical Research (Northampton). 3(Suppl. 3):101-104, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which comparisons were drawn between the types of patients presenting with psychiatric illness to hospital and general practitioner service. The differences highlighted included diagnostic labels and prognosis, and yet it was pointed out that the drugs used in the two situations are the same, although they may be used at different dose levels. The methodology of clinical trials in general practice was discussed, and reasons were given for the necessity of carrying out such trials on psychotropic drugs. 5 references. (Author abstract modified)

229078 Constant, J.; Dubois, J. Sevrey, F 71100 Chalon sur Saone, France **/Discourse on the double-blind method. Institution and experimentation: 19366-RP./** Discours sur la methode double aveugle. Institution et experimentation: 19366 RP. Revue de Neuropsychiatrie Infantile etc. (Paris). 23(5-6):329-343, 1975.

The double-blind study of the neuroleptic 19366-RP is reported, focusing on the relationships in the institution where the drug was used. A study of the behavior of the nurses indicated a series of sociological relationships that would be

threatened by the experiment: the nurse/child, nurse/doctor, and doctor/product studied relationships. The results confirm the neuroleptic and disinhibiting action of 19366-RP. The paradoxical successes (projected placebo effects) suggest the hypothesis of a relational functioning continually threatened by breakdown according to the type of relationship between partial objects. Joint research on the product's effects can thus be used as a means of understanding the pathological condition of mentally deficient psychotic patients. (Journal abstract modified)

229438 Cooper, Thomas B.; Simpson, George M. Rockland Research Institute, Orangeburg, NY **Plasma/blood level monitoring techniques in psychiatry.** Psychopharmacology Bulletin. 11(4):18-20, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 techniques for monitoring plasma and/or whole blood levels of various psychotropic drugs and their metabolites were described, stressing that current interest in this area has resulted partly from the fact that clinical titration of the dosage of drugs has been hampered by lack of reliable parameters for quantitative evaluation. Recently developed techniques have led to experimentation on the existence of the therapeutic window; whether or not, by using a pharmacokinetic approach, prediction of the dosage can be developed; and whether or not the dosage required can be determined from a single blood sample collected at fixed time intervals after a single oral dose of medication. It was concluded that results of experiments using lithium were generally successful. 6 references. (Journal abstract modified)

229439 Turner, William J.; Turano, Patricia; Badzinski, Stanley. Research Division, Central Islip Psychiatric Center, Central Islip, NY **An attempt to establish quality control in determination of plasma chlorpromazine by a multilaboratory collaboration.** Psychopharmacology Bulletin. 11(4):20-21, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 attempts to establish quality control in determination of plasma chlorpromazine by a multilaboratory collaboration were described. Chlorpromazine (CPZ), chlorpromazine sulfoxide (CPZS)), mono and didesmethylchlorpromazine (Nor 1 CPZ and and Nor 2 CPZ, respectively) were added to two collections of calf plasma, one at concentrations approximating the lowest clinically effective level and one near that of beginning toxicity. Assay was conducted both by gas chromatography (GC), thin layer chromatography, and direct scanning microdensitometry. Results indicate that the use of internal standard in GC gives excellent accuracy and precision for CPZ, but less so for the other three compounds. The greatest accuracy and precision was achieved at low and high level spiking. Reults suggested that this must be considered the standard which other methods must equal or surpass before they can be accepted. 7 references. (Journal abstract modified)

229441 Kaul, Pushkar N.; Clark, Mervin L. University of Oklahoma Health Sciences Center, Oklahoma City, OK **A novel approach to quantitative determination of subnanomoles of psychoactive drugs in blood.** Psychopharmacology Bulletin. 11(4):23-25, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 a new approach to quantitative determination of subnanomoles of psychoactive drugs in the blood was described. The method was tested with chlorpromazine (CPZ) and other tertiary amine psychoactive drugs. The extraction process from blood involved rendering a 3ml sonicated sample to pH 13 plus or minus .05 and extracting with 10ml n-hexane containing 1.5% isoamylalcohol. Transfer of the extract residue to the reaction microtube was accomplished through multiple transfers, and the residue was again evaporated to dryness for quaternization. Quaternization of the tertiary amine base was accomplised by adding 0.1ml of 0.04 mM solution of 9-bromomethylacridine in acetonitrile and 50mg of 20 micrometers of glass beads to the microtube containing the extract. Without modification, the method was capable of assaying as low as 20-30 ng/ml CPZ and CPZ sulfoxide and was applied to preliminary clinical studies with CPZ attempting to correlate blood concentrations of CPZ with clinical response. 17 references. (Journal abstract modified)

229442 Craig, J. Cymerman; Gruenke, Larry D. Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA **A contribution to psychoactive drug measurement techniques.** Psychopharmacology Bulletin. 11(4):25-27, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December 1974 recent development in combined gas chromatography/mass spectormetry (GC/MS) which have led to an increase in the sensitivity, accuracy, and biomedical utility of mass spectrometric assays were reviewed briefly. A new technique which involves addition of the accelerating voltage alternator, subsequently modified to the multiple ion detection (MID), has been developed which adds greatly to the sensitivity and accuracy of the GC/MS procedure, and has potentital usefulness in biomedical applications. Other advances include improved use of natural isotopic clusters in drug studies through applying compounds labeled with deuterium or carbon 13 and a new method of ionization (termed chemical ionization). An analog of the MID system has also been developed in which focusing is accurately maintained by means of voltage sweeping 9VS) using a variable superimposed sine wave voltage, and the application of MID/VS to biomedical problems is illustrated. 17 references. (Journal abstract modified)

229554 Cassano, Giovanni Battista; Castrogiovanni, Paolo; Placidi, Gian Franco; Carrara, Stefano. Universita degli Studi di Pisa, Istituto di Clinica Psichiatrica, Pisa, Italy **/Clinical experimentation of the long-acting neuroleptics: methodological problems./** Sperimentazione clinica dei "long acting". Problemi metodologici. Rivista di Psichiatria (Roma). 10(1):58-73, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, methodological problems involved in clinical experimentation with long-acting neuroleptic agents were discussed. These agents do not always lend themselves to the application of rigid experimental designs, or to the adoption of standardized evaluational criteria of the type commonly used in traditional controlled tests; independent variables seem to assume greater weight in this area. The difficulty of finding homogeneous and representative samples, the problems connected with evaluating therapeutic effects, the duration of treatment with consequent possibilities of changes in the social/environmental situation and other significant parameters of the patient's life, can compromise the validity of the results in the experiment. 40 references.

229906 Cano, J. P.; Baille, A. M.; Viala, A. Laboratoire de Toxicologie generale et Biotoxicologie, Faculte de Pharmacie, 27, Bd Jean Moulin, F-13 005 Marseille **Determination of bromazepam in plasma with an internal standard by gas-liquid chromatography.** Arzneimittel-Forschung (Aulendorf). 25(7):1012-1016, 1975.

A gas chromatographic assay method is described for the determination of bromazepam using methylbromazepam as internal standard. After alkaline ether extraction the bromazepam and methylbromazepam obtained from sulfuric acid reextraction are hydrolyzed to 2-amino-5-bromobenzoylpyridine (ABBP) and to 2-methyl-amino-5-bromobenzoylpyridine (MABBP), respectively. After neutralization, the bromo-pyridine-benzophenones are extracted with ether and dissolved in hexane after evaporation of the ether. Under the described gas chromatographic conditions, it was found that MABBP and ABBP have retention times of 10.5min and 12.5min, respectively. The limit of sensitivity is situated at 5ng/ml of plasma. The specificity is satisfactory since the metabolite which might have interfered (hydroxy-3-bromazepam) appears at very low concentrations in the blood. The linearity of the calibration curve was confirmed for plasma concentrations up to 100ng/ml. 3 references. (Author abstract)

230866 Seifert, R.; Bremkamp, H.; Junge, C. Neurochemisches Laboratorium der Psychiatrischen un Nervenklinik, Universitat Hamburg, D-2000, Hamburg, Germany **/Simplified lithium dose adjustment by load test./** Vereinfachte Lithiumeinstellung durch Belastungstest. Psychopharmacologia (Berlin). 43(3):285-286, 1975.

In a study of lithium dose adjustment, it is suggested that the lithium blood level 24 hrs after a priming dose of lithium is a prognosticator for the therapeutic dosage required. Exactly 24 hrs following the intake of 24 mval lithium (lithium carbonate, retard form) venous blood serum is analyzed for lithium content. The necessary therapeutic dose can be inferred from a regression line which shows the negative interrelation between the 24 hr value and the therapeutic quantity of lithium necessary to achieve a blood level of 0.9mval/1 under steady state conditions. Low 24 hr levels require high maintenance doses and vice versa. This procedure shortens the time of dose adjustment and avoids undesirable side-effects in the beginning of treatment which otherwise interfere with patient compliance in lithium therapy. 3 references. (Author abstract)

17 MISCELLANEOUS

225721 Katz, Martin M.; Itil, Turan M. Clinical Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20852 **Video methodology for research in psychopathology and psychopharmacology: rationale and application.** Archives of General Psychiatry. 31(2):204-210, 1974.

A method for recording interview behavior and patient's reaction to neuroleptic or psychotropic drugs by means of a videotape is described. This system is based on advances in the development of standard rating schedules, and is designed to increase reliability of ratings, to emphasize the measurement of nonverbal, expressive aspects of behavior, and to enhance the capacity of observers in the exercise of clinical judgment. Its sensitivity was tested by comparing it with a conventional rating procedure in a clinical trial involving the use of two drugs with different chemical structures but presumed to have similar actions. The video method showed increased sensitivity in detecting systemic differences in behavioral effects between the agents. 20 references. (Author abstract modified)

225869 Brown, Fountaine C.; Coleman, James H. P.O. Box 4966, Memphis, TN 38104 **Dopamine-beta-hydroxylase in nerve function and mental illness.** Diseases of the Nervous System. 36(7):383-385, 1975.

Literature and research on the role of dopamine-beta-hydroxylase (DBH) in nerve function and mental illness is reviewed and discussed. The most consistent observation in studies designed to evaluate the effects of acute and chronic stress and disease on serum DBH activity in humans is that a wide range of values is found among normal individuals; this normal variability in serum DBH concentrations in humans, which appears to be related to genetic factors, makes data derived from this system difficult to interpret. Other factors contributing to inconsistent data and conflicting reports on the reliability of DBH concentration as an index of sympathetic function are differences in assay techniques and timing of sampling. It is noted that the disparity of data has led to the suggestion that serum DBH analyses cannot be used to detect neuropsychiatric disorders. 39 references.

226877 von Schenck, Henning. Kliniskt-kemiska Centrallaboratoriet, Malmo allmanna sjukhus, 21401 Malmo, Sweden **/Unexpected laboratory results' effect on psychopharmacology./** Ovantade laboratorieresultat orsakade av psykofarmaka. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(2):95-106, 1974.

The concerns of laboratory analysts in assisting psychiatrists are discussed, and a comprehensive chart of 30 major neuroleptic, antidepressant, sedative, barbiturate, and antiepileptic drugs analyzed in laboratory studies is presented. Psychiatrists may question analysts regarding somatic symptomatology, toxic effects of particular drugs, chemical - technical interference which may hamper later analyses, and possible biochemical causes for somatic symptoms. Laboratory methods and research contributions in the study of pharmacological effects and chemical interference are reviewed. 99 references.

226961 Costa, E.; Greengard, P. no address **Advances in biochemical psychopharmacology.** New York, Raven Press, 1974. 4 volumes.

Volume 9, titled "Phenothiazines and structurally Related Drugs", Volume 10, titled"Serotonin -- New Vistas: Histochemistry and Pharmacology", Volume II, titled "Serotonin - New Vistas: Biochemistry and Behavioral and Clinical Studies", and Volume 12, titled "Neuropsychopharmacology of Monoamines and Their Regulatory Enzymes" are reviewed. The histochemistry and pharmacology of the phenothiazines and serotonin are described. The neuropsychopharmacology of monoamines and their regulatory enzymes are examined. 6 references.

227209 Lader, M. H. Institute of Psychiatry, University of London, England **The clinical pharmacology of anti-depressives.** Journal of International Medical Research (Northampton). 3(Suppl. 3):31-40, 1975.

At the International Vivalan Symposium, held in London in November 1974, a paper was presented in which the clinical pharmacology of antidepressives was discussed. The tricyclic antidepressives can be divided chemically into the tertiary amine compounds such as imipramine and amitriptyline, and the secondary amines, for example, desipramine and nortriptyline. The tertiary compounds are usually metabolized by N-dealkylation to a secondary compound, the latter eventually being present in the higher concentration. The relationship between plasma concentrations of tricyclics and clinical response is disputed. There is no agreement concerning the relationship between plasma tricyclic concentration and unwanted effects. The mode of action of these drugs also remains conjectural, although the weight of evidence now points to the relevance of the blockade of the reuptake of neurotransmitters, serotonin and noradrenaline. The tertiary tricyclics interfere mainly with serotonin uptake, the secondary compounds with noradrenaline. Clinically, the tertiary compounds are more effective against agitated types of depression; retarded depressives respond better to the secondary tricyclic antidepressives. The biochemical correlates of depression, however, remain unclear. 51 references. (Author abstract modified)

227411 no author. no address **Lithium -- futility, disaster and triumph.** Medical Journal of Australia (Sydney). 1(22):669, 1975.

A brief history of the use of lithium and lithium chloride is presented. First introduced in the mid-19th century, lithium was used as a remedy for gout, rheumatism, epilepsy and neoplasms, without realization of its psychotherapeutic properties. In the 1940s, lithium and salts were used as sodium chloride substitutes for congestive cardiac failure victims with fatal results. In 1949, the drug was recognized as a therapeutic substance and, in 1970 was reintroduced by the U.S. Food and Drug Administration for the treatment of mania. Lithium is presently used in the treatment of manic episodes, depressive swings of bipolar affective illness, manic-depressives, cyclothymia, and schizophrenia and schizoaffective illness. It is noted, however, that although the drug is an effective tranquilizer, it seems to have no effect on the schizophrenic process itself. 4 references.

227412 no author. no address **Drug interactions.** Medical Journal of Australia (Sydney). 1(22):669-670, 1975.

The unsatisfactory state of knowledge about drug interactions is discussed. It is noted that, due to the immense variety and types of drugs available, it is almost impossible to empirically formulate a list of interactions between them. With the

knowledge of drug interactions at such a limited level, and in the light of unsatisfactory testing done on animals, it is felt that the few known interactions based on adequate data have not yet made much impact on the medical world. It is concluded that the addition of an ineffective drug may result in unwanted interactions with other agents, and that stopping an unnecessary drug may be a major and positive act on the patient's behalf. 3 references.

227461 Olsen, M. Rolf. University College of North Wales, Wales **The non-contribution of drugs to the discharge of the long-stay psychiatric patient.** Social Work Today (Birmingham). 6(1):11-13, 1975.

Assumptions that drugs have enabled the successful treatment of the chronic long-stay patient in the hospital and have facilitated his discharge to and management within the community were tested in light of the Australian policy adopted in 1964 to discahrge such patients from a state hospital. Evidence shows that use of tranquilizing drugs made little impression upon the patients' hospital care or aided their return to the community. Patients still remained in the outdated, overcrowded back wards of the hospital, with little change in their traditional care. Decisions to release them to the community were not affected to any degree by drug regimes. More importantly, discharge decisions were often made without any knowledge of the outcome of the new policy or whether or not it was in the best interests of the patient, his family, or the community. There are moral issues implicit in such action, and the effects of the policy on both the community and the patient require urgent evaluation. 15 references.

227560 Stimmel, Glen L. University of Southern California, Los Angeles, CA 90007 **Clinical pharmacy practice in a community mental health center.** Journal of the American Pharmaceutical Association. 15(7):400-401, 418, 1975.

Because schools of pharmacy have made a major commitment to teaching clinically oriented pharmacy, it is essential that roles develop that will utilize this training. Funding of clinical pharmacy roles by nonpharmacy sources is a major step in the development of viable clinical pharmacy practice. A role model for clinical pharmacy practice in a community mental health center, funded by the City and County of San Francisco through District V Mental Health Center, is described. Efforts must be made to continue documentation and development of new roles, both by educating pharmacists as well as other professsionals of the present and potential state of clinical pharmacy practice. 8 references. (Author abstract modified)

227731 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD **Guidelines for antipsychotic drug use.** Resident and Staff Physician. 21(9):165-172, 1975.

Guidelines of the selection and administration antipsychotic drugs at different stages of the patient's treatment are presented, based on a plan that narrows the choice to five drugs: one each of the three classes of phenothiazines, a butyrophenone, and a thioxanthene. Dosage recommendations are given for acute psychotic states and maintenance treatment. Also discussed are the advantages of drug holidays, the negative effects of prolonged use of antipsychotic medication, frequency of daily doses, antiparkinson drugs, medication after discharge, and long-acting injectables. 10 references.

227761 Kristjansen, Palle. Set Hans Hospital, Dept H, DK-4000 Roskilde, Denmark **Scandinavian standpoint on the Liege classification of neuroleptics.** Acta Psychiatrica Belgica (Bruxelles). 74(5):462-469, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the Scandinavian view of the Liege classification of neuroleptics was discussed. It was suggested that such a classification system may be of some use for those engaged in sophisticated research in clinical psychopharmacology, but not useful in daily practice. The similarities between neruoleptics are considerably more important than the differences. It was also contended that the stellar configuration is too confusing; the bipolar model appears to be easier to use.

227769 Bobon, Daniel P.; Gottfries, Carl G. Department of Psychiatry, University of Liege Medical School, Rue St. Laurent 58, B-4000, Liege, Belgium **The Liege physiognomy of neuroleptics, with special reference to thioxanthenes.** Acta Psychiatrica Belgica (Bruxelles). 74(5):535-544, 1974.

At the first joint meeting of the Scandanavian and Belgian Societies of Psychopharmacology, held in Liege in June 1973, the Liege physiognomy of neuroleptics was reviewed. The nature of the various parameters, including the ataraxic effect, the antimanic effect, the antiautistic effect, the antidelusional effect, the extrapyramidal side-effect, and the adrenolytic effect were analyzed. Therapeutic dosage and effects of chlorprothixene, clopentixol, flupentixol hydrochloride and tiotixene were summarized.

228211 Kazamatsuri, Hajime; Kato, Shinsho. Department of Psychiatry, Teikyo University School of Medicine, Tokyo, Japan **New drug therapy in the field of psychiatry.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1293-1305, 1974.

Psychopharmacological studies on 13 newly marketed psychotropic drugs in Japan during 1970-1974 are reviewed. The chemical synthesis, effects and side-effects of spiclomazine, thiothixene, flupentixol, pimozide, oxypertine, clothiapine, clocapramine, clomipramine, nortriptyline, oxazolam, medazepam, and cloxazolam are considered. Application of nonpsychotropic drugs in the treatment of mental illness is discussed, including large doses of vitamins for treatment of schizophrenia, L-dopa for schizophrenia, amine precursor treatment for depression, beta-blocking agents for depression and dephenylhydantoin for psychomotor excitation. 127 references.

228244 Krakowski, Adam J. 210 Cornelia St., Suite 103, Plattsburgh, NY 12901 **Non specific factors in psychopharmacotherapy.** Psychosomatics. 16(3):132-134, 1975.

The importance of nonspecific factors of psychopharmacotherapy in the treatment of mental illness was discussed. The psychosomatic model of treatment, which follows the understanding that the causes of mental illness are multiple, was described in relation to its use of biological and psychosocial approaches to treatment. The nonspecific factors in psychopharmacology relate to the psychosocial components of illness. These factors, especially the placebo effects, were considered to be as important as the pharmacological influences, and it was felt that they should be understood before any chemotherapy of mental illness is undertaken. 13 references. (Author abstract modified)

228309 Yanagida, Tomoji. Department of Psycho-pharmacology, Jikken Dobutsu Chou-kenkyujo Research Institute, Kawasaki, Japan **Recent views in psychopharmacology: behavior pharmacological aspects.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1281-1286, 1974.

Recent research on behavioral pharmacology in psychiatry is discussed. Factors which constitute behavior, the role of operant behavior in animal experiments in behavior pharmacology, and factors which affect behavioral effects of drugs are considered. Advantages of behavioral pharmacology in studies on drug dependence and drug effects on senses are also described. 9 references.

228322 Goto, Yoko. Shikiba Hospital, Ichikawa, Japan **Issues concerning drug therapy in the mental hospital.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1307-1312, 1974.

Problems in psychopharmacotherapy in a private mental hospital are discussed. Private mental hospitals are often forced to receive chronic patients, emergency patients, and those patients who are difficult to handle, since public hospitals often refuse to accept such patients using as an excuse lack of sufficient facilities and psychiatrists. Private mental hospitals also lack well qualified psychiatrists and a large number of patients with various types of problems are treated by a small number of poorly qualified psychiatrists. Due to high costs of newly developed effective psychotropic drugs, private hospitals tend to use cheaper, less effective drugs. It is noted that families of patients and patients themselves have the wrong idea that private mental hospitals sell larger amounts of more expensive psychotropic drugs in order to make larger profits. 8 references.

228323 Yagi, Gohei. Minagawa Hospital, Kanagawa, Japan **Worldwide trends in the psychopharmacological studies.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(12):1327-1334, 1974.

Activities of the Ninth Collegium International Neuropsychopharmacologicum are summarized. The number of participants from each country, the names of major participants, the topics for discussion, and the names of new psychotropic drugs are included.

228978 Klein, Donald F.; Ross, Donald C.; Feldman, Sydney. Research Dept., Hillside Div., Lond Island Jewish-Hillside Medical Center, NY **Analysis and display of psychopharmacological data.** Journal of Psychiatric Research (Oxford). 12(2):125-147, 1975.

The assumptions underlying ANOCOVA (analysis of covariance) are reviewed and their relationship to psychopharmacological data distributions stated. An alternative method of analysis that makes fewer assumptions, such as partition of contingency tables, would be desirable, with cohens kappa statistic providing a suitable basis for an alternative method. An a priori method of searching for drug typical changes is described. This method of defining drug typical and placebo typical pre to post symptom change patterns by maximizing kappa is demonstrated. The necessary formulas for calculating kappa and performing a chi-square test for the significance of kappa in the 3 dimensional case have been presented. Examples comparing ANOCOVA with maximization of kappa and an alternative partitioning method have been presented and similarities and differences in results pointed out, emphasizing the value of this method for easy comprehensible display of drug effects. 23 references. (Author abstract modified)

229043 Chrusciel, L. Office of Mental Health, World Health Organization, Geneva, Switzerland **Recent progress in the long-term pharmacological research on cannabis.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 12(1/2):57-62, 1975.

Rapid increase in the knowledge of acute biological effects of cannabis and its biologically active components is contrasted with the slow rate of progress achieved in the area of effects of long-term use of cannabis in man. Such studies belong to the difficult category of long-term clinical pharmacological studies that are time consuming, require large population samples and considerable staff expertise. Recently published epidemiological studies on effects of long-term cannabis use, although still not conclusive, supply increasing evidence of harmful effects of such use. Research projects sponsored by the World Health Organization in countries with easy access to long-term heavy cannabis users are outlined. 26 references. (Author abstract modified)

229112 Chrusciel, T. L.; Chrusciel, M. World Health Organization, Geneva, Switzerland **Selected bibliography on detection of dependence-producing drugs in body fluids.** Geneva, World Health Organization, 1975. 67 p. 15 Sw. francs.

A comprehensive list of recent analytic methods that can be used to detect dependence producing drugs in the body is presented on the basis of scientific literature published between 1969 and 1974. The multilingual bibliography includes articles on methodological problems; methods; detection of opiates and synthetic narcotic drugs; detection of opiate antagonists; amphetamines and amphetamine like substances; cocaine; ephedrine; and barbiturates and other sedative and hypnotic drugs, including tranquilizers. References also deal with detection of cannabis, hallucinogens and volatile substances. 1057 references.

229240 Group for the Advancement of Psychiatry. 419 Park Avenue South, New York, NY 10016 **Pharmacotherapy and psychotherapy: paradoxes, problems and progress.** New York, Group for the Advancement of Psychiatry, 1975. 167 p. $6.00

Crucial problems and issues concerning the interrelationship of drugs and psychotherapy are explored in a position statement by the Group for the Advancement of Psychiatry. Consideration is given to American psychiatry's reaction against orthodox psychoanalytic concepts, the value of symptom removal as the basis for the curative process, and the need for more research in the field of psychobiology.

229349 Safra, Mark J.; Oakley, Godfrey P., Jr. Cancer and Birth Defects Div., Bureau of Epidemiology, Center for Disease Control, Atlanta, GA 30333 **Association between cleft lip with or without cleft palate and prenatal exposure to diazepam.** Lancet (London). 2(7933):478-480, 1975.

Interviews from 278 women who had infants with selected major malformations were reviewed. A history of diazepam ingestion in the first trimester of pregnancy was found to be four times more frequent among mothers of children with a cleft lip with or without a cleft palate than among mothers of children with other defects. This association was one of many examined in the analysis, suggesting chance results, but this report is the second one linking diazepam to cleft lip with or without cleft palate. It is concluded that until there are more data available on this question, the possible risk should be considered when prescribing diazepam for women in their productive years. 7 references. (Author abstract modified)

229452 Tuma, A. Hussain. Clinical Research Branch, NIMH, Rockville, MD 20852 **Conceptual implications of drug and nonsomatic treatment interaction studies.** Psychopharmacology Bulletin. 11(4):42,44, 1975.

At the Thirteenth Annual Meeting of the ACNP, held in San Juan, Puerto Rico in December, 1974, the differential role and efficacy of drugs and psychosocial therapies with major mental disorders were discussed. It was stressed that: (1) it seems profitable to look for differential contributions from drugs and from psychotherapy; (2) there is a need to distinguish between immediate results from drugs and the delayed results from psychotherapy; (3) the needs and demands of each phase of a given disorder must be considered; (4) focus must be on both psychological treatments used in these studies and the specific criteria used in assessing social adjustment; (5) there is a need to further differentiate among subgroups of patients when determining use of information and techniques now available in the area of psychopathology; and (6) the inadequacies of traditional sampling and data analytic models, assumptions, and concepts and the procedures associated with them must be addressed. 9 references. (Journal abstract modified)

229552 Bogliolo, Corrado; Suman, Antonio; Cossidente, Alberto; Catagni, Carlo Federico. Servizi Psichiatrici Provinciali, Florence, Italy **/The social-familial reinsertion of the psychotic patient through the use of long-acting neuroleptics./** Il reinserimento socio-familiare del paziente psicotico mediato dalla utilizzazione dei neurolettici long acting. Rivista di Psichiatria (Roma). 10(1):44-53, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, the reinsertion of the psychotic patient into society through the use of long-acting neuroleptic agents was discussed. These drugs induce favorable conditions for an interpersonal approach and provide the basis for individual or group psychotherapy, in addition to their specific neuroleptic effect. Other advantages of these drugs include the fact that a constant dosage level can be established, and the fact that they can be administered only once a month in relatively small amounts. Use of long-acting neuroleptics combined with psychiatric support is successful in reintegrating the psychotic patient into his family and social environment. 21 references.

229553 Campailla, Giuseppe; Bonfigli, Luisa. Universita digli Studi di Trieste, Italy **/Sociopsychiatric aspects of long-acting neuroleptics./** Aspetti socio-psichiatrici dei neurolettici ad azione prolungata. Rivista di Psichiatria (Roma). 10(1):54-57, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, social psychiatric aspects of long-acting neuroleptic drugs were discussed. At present, the goal of psychiatric care for the mentally ill is treatment outside the institution; the use of long-acting neuroleptic agents is one of the most important factors in accomplishing this goal. These agents reduce the period of hospitalization and decrease the possibilities of rehospitalization. The side-effects of long-acting neuroleptics are no greater than the side-effects encountered with orally administered neuroleptic agents. The introduction of long-acting neuroleptic drugs in therapy represents a milestone in restoring freedom to the mental patient.

229555 De Maio, Domenico. Centro Pronto Intervento per Malattie Nervose e Mentali "Riccardo Bozzi", Via Assietta 38, Milan, Italy **/Psychometric clinical evaluation, through Overall and Gorham's test, of therapy with fluphenazine decanoate./** Valutazione clinico psicometrica, mediante reattivo di Overall e Gorham, della terapia con flufenazina decanoato. Rivista di Psichiatria (Roma). 10(1):74-78, 1975.

At the First National Symposium on Long-acting Fluphenazine, held in Rome in October 1974, the clinical psychometric evaluation of treatment with fluphenazine decanoate was discussed. Fluphenazine decanoate (FD) is particularly indicated in psychoses. It is suitable for instrumental control of therapeutic results, such as Overall and Gorham's scale, and large doses are not necessary for obtaining good effects. The dystonic extrapyramical syndrome which sometimes occurs with administration of this drug is not particularly serious and long-lasting. In addition, it does not present ethical problems which differ from those encountered with any type of treatment. 9 references.

229558 Patarnello, Ludovico. Ospedale Psichiatrico Provinciale di Padova, Padva, Italy **/The position of long-acting drugs in the economy of psychiatric institutions./** La Posizione degli psicofarmaci ad azione ritardo nell'economia delle istituzioni psichiatriche. Rivista di Psichiatria (Roma). 10(1):92-104, 1975.

At the First National Symposium on Long-acting Fluphenazine held in Rome in October 1974, the capacity for change of psychiatric institutions and the position that psychopharmacology can assume in the logic of institutional behavior were discussed. There are two types of change: one occurs inside a given system which remains unchanged; the other changes the system itself. Despite the wide use of drugs in the psychiatric institution, which were supposed to cause changes of the second type, the changes possible in the context of present psychiatric institutions are of the first type. Psychiatric institutions use drugs badly, or at least use them primarily for control of the inmates. The most positive aspect lies in leaving the patient more time and a more natural space (outside the hospital) for organizing a personal and more radical change.

229561 Vinci, M. Ospedale Psichiatrico Provinciale "Leonardo Bianchi", Universita di Napoli, Naples, Italy **/Fluphenazine decanoate in association with other psychotropic drugs (preliminary note)./** Il decanoato di flufenazina in associazione con altri psicofarmaci (nota preliminare). Rivista di Psichiatria (Roma). 10(1):122-124, 1975.

At the First National Symposium on Long-acting Fluphenazine held in Rome in October 1974, the use of fluphenazine decanoate in association with other drugs was discussed. In association with butyrophenones, thioxanthenes, and some phenothiazine derivatives such as triflupromazine, and trifluperazine, the association provoked the earlier and less controllable appearance of parkinsonian disturbances, reinforcement of secondary psychopathological interference, and in no case improved the clinical picture. Similar effects were encountered with association with haloperidol, clopenthixol and thiotixene. Combination of the drug with sedatives was effective especially in schizophrenia with disturbances of excitement; good synergism was encountered with promazine, levopromazine, perphenazine, thioridazine and chlorpromazine.

229852 Woody, George E.; O'Brien, Charles P.; Greenstein, Robert. VA Hospital, 39th and Woodland Avenues, Philadelphia, PA 19104 **Misuse and abuse of diazepam: an increasingly common medical problem.** International Journal of the Addictions. 10(5):843-848, 1975.

Misuse and abuse of diazepam among addiction prone individuals is reported. The most common pattern of abuse is periodic ingestion of 30mg to 80mg of diazepam in one dose, either alone or in conjunction with methadone or other narcotics. Two cases of physical dependency to diazepam are re-

ported. Many addict patients using diazepam are buying it on "the streets."All physicians should know that diazepam abuse and misuse is occurring, and careful attention should be given to prescribing, transporting, and storing this drug. 9 references. (Author abstract)

230118 Davies, Brian. University of Melbourne, Royal Melbourne Hospital, Victoria, 3050, Australia **Getting psychiatric patients to take their medication.** Current Therapeutics (Milford). 16(4):11-12, 15, 1975.

Research indicates that psychiatric patients do not necessarily take prescribed drugs as directed. One study of the reluctance of 46% of schizophrenic patients to take their medication is cited, indicating extrapyramidal involvement as one cause of patients' reluctance. Practical clinical points related to patients' reluctance to take drugs are enumerated and suggestions are offered to alleviate this problem. Further research of patients' attitudes towards their drugs and doctors, and of doctors' attitudes towards drugs and side-effects are recommended. 1 reference.

230119 Johnson, Gordon. Department of Psychiatry, University of Sydney, Australia **Clinical use of drugs for sleep disturbances.** Current Therapeutics (Milford). 16(5):15-16, 1975.

The restorative powers of sleep, the need for sleep, varying disturbances of sleep pattern and the effectiveness and side-effects of sleep producing drugs are discussed. The ideal hypnotic should not interfere with physiological sleep patterns, should produce rapid induction and maintenance of sleep, should have no associated morning hang-over, should show low tolerance and dependence liability, and should have a minimal potential for drug interactions. The barbiturates which have been the most commonly prescribed hypnotics score badly on this profile. The benzodiazepines appear to be the safest of the presently available hypnotic drugs, and flurazepam has been shown to maintain its effectiveness over 2 weeks of treatment. Other classes of psychotropic drugs, such as the phenothiazines and tricyclic antidepressants, produce variable degrees of sedation and may show sleep inducing effects. 1 reference.

230640 Aleksandrowicz, Jerzy W. Klinika Psychiatryczna AM im. M. Kopernika, Krakow, Poland /**Pharmacotherapy and psychotherapy in the treatment of neuroses.**/ Farmakoterapia i psychoterapia w leczeniu nerwic. Psychoterapia (Krakow). 10:3-6, 1974.

Pharmacotherapy and psychotherapy are discussed as essentially analogical means of treatment for neuroses. The sources of the opposition between the two forms of therapy are found in the contrast between the biological, medical, cultural and psychosocial manners of thinking about the patient and the disease. Attention is called to the fact that the theory promulgated by Freud contains more elements of the dialectical formulation of the unity of contradictions than do the views of contemporary therapists. It is emphasized that the treatment of a neurotic patient requires that his psychophysical being be influenced in relation to his environment. 11 references. (Journal abstract modified)

231019 van Kammen, Daniel P. NIH Clinical Center, Room 4N214, Bethesda, MD 20014 **GABA and the dopamine hypothesis of schizophrenia.** Bethesda, NIMH, 1975. 20 p.

Studies were designed to investigate whether there is an imbalance in the gamma-aminobutyric acid (GABA) mediated function in schizophrenia which can be linked to the postulated hyperactive dopamine system. The close anatomical presence and biochemical interactions between GABA andd dopamine systems makes GABA a likely candidate for the hypoactive or imbalanced antagonistic neurotransmitter system postulated to induce a hyperactive dopamine system hypothesized to exist in schizophrenia. Strategies that are directed to this question and compounds that may be used to increase GABA and decrease dopamine activity at the neuronal sites are discussed. 63 references. (Author abstract modified)

231021 Greengard, Paul. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Cyclic nucleotides, protein phosphorylation, and neuronal function.** In: Drummond, G., Advances in nucleotide research. New York, Raven Press, 1975. (p. 585-601), v. 5.

Studies concerning the possible involvement of cyclic nucleotides and protein phosphorylation in the function of the nervous system and certain nonneuronal tissues are reviewed. Findings suggest that the actions of certain neurotransmitters at some synapses may be mediated through cyclic adenosine 3′,5′-monophosphate (cyclic AMP), and the actions of other neurotransmitters at other synapses may be mediated through cyclic guanosine 3′,5′-monophosphate (cyclic GMP). The mechanisms by which cyclic AMP and cyclic GMP mediate the effects of neurotransmitters and of hormones on membrane permeability, in both neural and nonneural tissues, may involve regulation of the state of phosphorylation of specific proteins present in the plasma membranes of the responsive tissues. 40 references.

231112 Sudilovsky, A.; Gershon, S.; Beer, B. no address **Predictability in psychopharmacology: preclinical and clinical correlations.** New York, Raven Press, 1975. 370 p. $22.50.

New insights into the problems encountered both at the preclinical and the clinical level of determining the pharmacologic properties of new drugs are presented, interim measures are proposed, and new procedures and hypotheses are explored. The difficulties inherent in the clinical phase of assessment are emphasized, and practical suggestions for making progress toward overcoming these difficulties are offered. Possible new methods and concepts are presented in the specific area of predicting drug activity.

231113 Simpson, Lance L. no address **Drug treatment of mental disorders.** New York, Raven Press, 1975. 425 p. $19.75.

Drugs that are used often and with notable therapeutic success in the treatment of mental disorders are discussed. Each drug is described in accordance with current knowledge of its basic and clinical pharmacology. Those aspects of drug action which have therapeutic significance are emphasized and, wherever appropriate, there is a discussion of current concepts of the biological basis of mental disorders to emphasize the idea that specific drugs should be used to remedy or offset specific disorders. Drugs discussed are: phenothiazines, thioxanthenes, haloperidol, butyrophenones, benzodiazepines, meprobamate, propanediols, tricyclic antidepressants, monoamine oxidase inhibitors, amphetamines and related stimulants, lithium, and rubidium. Mental disorders discussed are schizophrenia, depression, anxiety, and mania.

231227 Abel, Ernest L. Research Institute of Alcoholism, NY **Drugs and behavior: a primer in neuropsychopharmacology.** New York, John Wiley & Sons, 1974. 229 p. $13.95.

The effects of drugs on behavior are reviewed from a neuropsychopharmacological viewpoint. Topics covered include:

1) the structural and functional basis of behavior; 2) biological factors affecting the activity of drugs; 3) mechanism of drug action; 4) the sources of variability in drug activity, including age, sex, genetics prior experience and motivation; and 5) pharmacology of the central nervous system. The psychopharmacology of the different synapses (cholinergic, adrenergic, and serotonergic) is also described and details are given on the major groups of psychopharmacological agents.

231410 Mendlewicz, J. New York, NY **Genetics and psychopharmacology.** New York, S. Karger, 1975. 132 p. Vol. 10. $14.25.

Individual variations for various psychoactive drugs in rate of drug biotransformation and drug response are examined with regard to genetic factors. Topics considered include: relationship of genetic factors to course and drug response in schizophrenia, mania and depression; alcoholism as a pharmacogentic disorder; genetic factors and lithium response in manic-depressive illness; the relationship between acetylator status and response to phenelzine; low platelet monoamine oxidase and vulnerability to schizophrenia; genetics of monoamine oxidase and vulnerability to schizophrenia; genetics of monoamine oxidase; the inhibition of monoamine oxidase; a genetic study of plasma dopamine beta-hydroxylase in affective disorders; the cytogenetic effects of psychoactive drugs.

231607 Ban, Thomas A. Dept. of Psychiatry, McGill University, Montreal, Quebec **Clinical psychopharmacology and psychiatry.** Diseases of the Nervous System. 36(11):612-616, 1975.

At the first conference of Latin American Society of Psychobiology, held in Sao Paulo, Brazil, in December 1973, psychiatric concepts and thoughts were evaluated as a result of developments in clinical psychopharmacology. The treatment of schizophrenia, affective disorders, and neuroses was emphasized. The four areas where clinical psychopharmacology will provide clinical services missing from the traditional structural organization of psychiatry, and which will provide training and research, were discussed: offices of general practitioners; consultation service of psychiatrists; diagnostic and therapeutic facilities in general hospitals; and specialized investigational and therapeutic units at universities. 21 references.

231749 Watts, Geoff. no address **CURB on barbiturates.** World Medicine (London). 11(2):25,27-29, 1975.

Barbiturate abuse and efforts by the Campaign on the Use and Restriction of Barbiturates (CURB) to control this abuse are discussed. CURB's major objections to barbiturates are that they provide too easy a means of self-poisoning; their takers unsuspectingly become habituated; and a considerable number of young people misuse them, sometimes with fatal results. It is noted that clinicians generally concur that the benzodiazepines are preferable to barbiturates in inducing sleep, the prime function of prescribed barbiturates. The difficulties in curbing barbiturate use are explored. CURB aims not to ban barbiturates but to make clinicians aware of the less damaging alternatives, an option which may be lost if increased barbiturate abuse necessitates legislative action.

232517 Carpenter, John A.; Marshman, Joan A.; Gibbins, Robert J. Center of Alcohol Studies, Rutgers Univ., New Brunswick, NJ 08903 **Drug interactions: the effects of alcohol and meprobamate applied singly and jointly in human subjects. I. Theoretical considerations and literature review.** Journal of Studies on Alcohol. Supplement No. 7:1-53, 1975.

The considerations necessary to describe the effects of combinations of drugs in a biological system are reviewed. These effects -- additive, potentiative, antagonistic, synergistic -- are discussed with respect to the mathematical models needed to define them. Research on the effects of alcohol and meprobamate and their interactions is reviewed, including behavioral and pharmacological studies and also some studies of the interaction of alcohol with other drugs. Attempts to describe complex physiological and biochemical processes which determine the relationship between administered and effective dose are further complicated by route of drug administration and various time relations. The descriptions of biochemical and physiological events seem well advanced; those of behavior are not. Much of the behavioral research assumes that a single dose is representative of all doses of the drug, and that combinations of the drugs and additivity of effects can be determined without a rigorous definition or means of application. 249 references. (Author abstract modified)

232545 Kiczak, Janina; Warnecka-Przbylska, Maria; Wdowiak, Maria. Klinika Psychiatryczna PAM, ul. Broniewskiego 1, blok 32, 71-460 Szczecin, Poland /**Two cases of psychic disturbances in visceral lupus erythematosus.**/ Dwa przypadki zaburzen psychicznych w toczniu rumieniowatym trzewynm. Wiadomosci Lekarskie (Warszawa). 28(20):1747-1751, 1975.

Two cases are reported of patients with visceral lupus erythematosus who developed transient psychic disturbances during the course of treatment. In the first case symptomatic psychosis of the paranoid syndrome type was diagnosed and in the other case symptomatic psychosis of the hallucinatory type followed by delusioned reaction was diagnosed. In both cases the doses of corticosteroids were reduced at the time of psychosis and psychotropics were given. The problem of psychic disturbances in this disease and diagnotic difficulties and treatment are discussed. 10 references. (Journal abstract modified)

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